Sutherland Simpson

The Russell Sage Institute of Pathology

IN AFFILIATION WITH

The Second Medical Division of Bellevue Hospital

CLINICAL CALORIMETRY

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Reprinted from the Archives of Internal Medicine, Vol. 15, Part II, May 15, 1915

CHICAGO
AMERICAN MEDICAL ASSOCIATION, FIVE HUNDRED AND THIRTY-FIVE N. DEARBORN ST.
1915

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CLINICAL CALORIMETRY

FIRST PAPER

A RESPIRATION CALORIMETER FOR THE STUDY OF DISEASE *

GRAHAM LUSK

Scientific Director, Russell Sage Institute of Pathology

NEW YORK

HISTORICAL

A respiration calorimeter is an apparatus designed for the measurement of the gaseous exchange between a living organism and the atmosphere which surrounds it, and the simultaneous measurement of the quantity of heat produced by that organism.

The first contrivance of this nature was described by Lavoisier in 1780. It will be remembered that Lavoisier was the first to comprehend the significance of the then newly discovered oxygen. Primitive though the apparatus, yet intellectually inspiring was the mind which so early grasped the principles and understood many of the difficulties.

Apparatus for the measurement of the respiratory exchange was perfected before that for the measurement of heat production. Thus, Regnault and Rieset[1] in 1850 designed an air-tight apparatus in which an animal was placed; the carbonic acid formed in it was removed by pumping the air into flasks filled with potash, and oxygen was added from time to time as it was required. This is the *closed circuit* system which in a modified form is used to-day.

The historic respiration apparatus of Pettenkofer[2] and Voit was completed in 1862. This machine was capable of measuring the carbon dioxid output of a man within 1 per cent. of error. As early as 1866 Voit began computing from the substances oxidized in the body the quantity of heat which should have arisen from the destruction of those substances. This method is known as *indirect calorimetry*.

In 1885, Rubner, working in Voit's laboratory, published results concerning the calorimetry of foods. Accurate determinations of the

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Regnault and Rieset: Ann. d. Chem. u. Pharmakol., 1850, lxxiii, 92, 129, 257.

2. Pettenkofer: Ann. d. Chem. u. Pharmakol. Supplement 2, 1862.

heat value of urea, and of dry urinary solids were made for the first time. This work established biological standards for the heat values of proteins, carbohydrates and fats which are to-day accepted.

About the same time a calorimeter for the measurement of the heat production in man was set up in Voit's laboratory and many experiments were made with it by Carl Voit and his brother Erwin Voit. The results were apparently not satisfactory, for nothing was ever published on the subject. At this time Atwater was in Voit's laboratory, and in 1888 published from that laboratory an article on the absorption of the flesh of fish.

Atwater's interest in nutrition had already been stimulated by Johnson and Brewer at Yale, and through studies in agricultural and physiological chemistry in Berlin in 1869-71. In 1877 he began investigations into dietary requirements of the people. It was Atwater's association with Voit and with Rubner, however, which gave him his knowledge of the principles of the subject of calorimetry as applied to the living organism. These facts, which are not widely known, emphasize again the overwhelming debt which American science owes to Germany.

In 1894 Rubner built the first successful respiration calorimeter. He built it largely with his own hands and with the very moderate means available in his laboratory at Marburg where he had become professor of hygiene. Voit, on hearing the news, said that it was the most important invention of its kind since the invention of the thermometer. Rubner's calorimeter, which measured the heat production of a dog, was associated with the mechanism of a Pettenkofer respiration apparatus which determined the carbonic acid output of the animal. Thus *indirect calorimetry* could be compared with *direct calorimetry*. For example, if the nitrogen in the urine and feces of a dog fed with meat and fat were determined, and this nitrogen were multiplied by 6.25, the quantity of protein destroyed could be estimated. Since each gram of protein yields 4.1 calories of heat in the body, the quantity of heat produced from protein would be

$$\text{Grams excreted N} \times 6.25 \times 4.1$$

To estimate the quantity of fat oxidized the quantity of carbon contained in the protein destroyed (which amounts to grams excreted N $\times$ 3.28) was deducted from the quantity of carbon contained in the

3. For the history of animal calorimetry see Rubner: Tigerstedt's Handbuch der physiol. Methodik. i, 150; Johansson, Abderhalden's Handbuch der biochem. Arbeitsmethoden, Berlin, 1910, iii, 1114.

excreta, that is, the sum of that in the urine, feces and respiration. The remainder represented the quantity of expired carbon derived from the oxidation of fat. Since fat contains 76.5 per cent. of carbon and 1 gm. of fat yields 9.3 calories, it was easy to calculate the heat production derived from fat. Recapitulating, one may express the heat produced from fat in the formula:

$$\text{Total C} - (\text{N} \times 3.28) \text{ divided by } 76.5 \times 100 \times 9.3$$

Adding together the heat calculated as that which should have arisen from the protein and fat metabolized, Rubner found that this sum was exactly the amount of heat given off by the animal as measured by the calorimeter. This was the first long-sought demonstration of the law of the conservation of energy applied to animal life.

After returning to America, Atwater in 1892 began work on a calorimeter which could measure the heat production in man. In 1894 the United States government began to appropriate funds for investigations into the nutrition of the people and placed the distribution of these funds in the hands of Professor Atwater. A portion was wisely used in the construction of the Atwater-Rosa[4] respiration calorimeter, the earlier description of which appeared in 1897. In 1893 C. F. Langworthy and in 1895 F G. Benedict became associated with the undertaking. Shortly after the completion of the apparatus, Rosa, the expert physicist, to whose skill its successful completion was largely indebted, retired from direct association with the enterprise, although, as professor of physics at Wesleyan he was still frequently consulted until, in 1901, he became chief physicist of the Bureau of Standards at Washington. The Atwater-Rosa calorimeter demonstrated that direct and indirect calorimetry agreed in man, not only during rest, but also during periods when mechanical work was performed.

The original Atwater-Rosa calorimeter was associated with a respiration apparatus of the type designed by Pettenkofer, which measured only the carbon dioxid output. Calculated on this basis the production of heat might show a maximum error of 24 per cent., depending on whether carbohydrate or fat was being oxidized. At a later date funds were granted to Atwater by the Carnegie Institution in order to apply the principle of the closed circuit of Regnault and Rieset to the apparatus so that the oxygen absorption might also be determined. The modification of the apparatus along these lines was begun in 1902, and the work accomplished during 1903 to 1905 was done during a period when Atwater was in full control of the undertaking. Atwater's illness

4. Atwater and Rosa: Report of the Storrs Agric. Exper. Station, 1897, p. 212.

began in 1905, his retirement took place in 1906 and he died in 1907.

With the improved apparatus, publication[5] concerning which fell in 1905, not only heat production and carbon dioxid output were accurately measured, but the absorption of oxygen as well. It thus became possible to measure not only the non-protein carbon in the respiration, but also to calculate how much of the oxygen absorbed was devoted to the destruction of non-protein material; that is to say, fat and carbohydrate. The value of this knowledge becomes apparent when it is realized that one liter of oxygen used for the oxidation of fat yields 4.686 calories, whereas when the same volume is used to oxidize starch 5.047 calories are set free, a difference of over 7 per cent. When carbohydrate is oxidized the volume of oxygen absorbed is equal to the volume of carbon dioxid expired and the *respiratory quotient* equals unity.

$$\text{R. Q. equals } \frac{\text{Vol. } CO_2}{\text{Vol. } O_2} = 1$$

When fat is oxidized, however, the respiratory quotient is only 0.70. Respiratory quotients (corrected from protein influence) which run intermediate between 0.70 and 1.00 are deemed to represent the oxidation of mixtures of carbohydrates and fats, and the heat value of a liter of oxygen varies accordingly. Thus a quotient of 0.85 represents the oxidation of fat and carbohydrate together in such a proportion that 49 per cent. of the calories produced are derived from carbohydrate and 51 per cent. from fat. Under these circumstances, 1 liter of absorbed oxygen represents 4.863 calories liberated in the organism. Tables giving these data were first published by Zuntz.[6]

The ability to determine the oxygen absorption with exactness abolished a possible error of considerable magnitude in the calculations of indirect calorimetry. This improvement brought the apparatus to a high degree of perfection. The Carnegie Institution of Washington has richly provided for the higher development of the work in the Nutrition Laboratory at Boston, which represents the realization of Atwater's ambition for the establishment of a separate laboratory for this work. Dr. Benedict is here the controlling genius, while the original Wesleyan calorimeter, now removed to Washington, is under the direction of Dr. C. F. Langworthy.

5. Atwater and Benedict: Carnegie Institution of Washington, 1905, Pub. 42. See also, Benedict and Carpenter: 1910, Pub. 123.

6. Zuntz and Schumburg: Studien zu einer Physiologie des Marches, Berlin, 1901. See also, Williams, Riche and Lusk (Jour. Biol. Chem., 1912, xii, 357), for other references.

ANIMAL CALORIMETRY AT THE CORNELL UNIVERSITY MEDICAL COLLEGE

At the time of my appointment to the professorship of physiology at the Cornell University Medical College, the authorities liberally provided for the construction of a respiration apparatus. Dr. Murlin spent a part of the summer with Dr. Benedict in Boston, where he freely received every privilege of the laboratory. After considerable discussion, I decided to have a calorimeter constructed which was small enough for use with dogs and babies, work which, up to that time, had not been included in the program of the Boston laboratory. The construction of this apparatus was entrusted to the capable management of Dr. H. B. Williams.[7] Full and grateful acknowledgment is due to Dr. F. G. Benedict, who has ever given all that counsel which his unique experience in calorimeter construction makes of highest value.

The problem of the measurement of 7 calories of heat produced in an hour by a baby weighing 3 kg. was different from that presented by the measurement of 70 calories produced by an adult. This led to the addition to the calorimeter of certain refinements in technical construction which are due to Dr. Williams. The small calorimeter has been successfully used in many experiments on dogs and babies. For the first time direct and indirect calorimetry were found to agree during hourly periods of experimentation.

The method employed with dogs was to determine the *basal metabolism* as measured by that quantity of heat which was produced by the resting animal when there was no food in the gastro-intestinal tract, and to compare this metabolism with that found at times following the ingestion of various foods. It was found that three or four hours of observation sufficed to indicate the influence of ingested food.

The satisfactory working of the apparatus used in accordance with these principles encouraged me to believe that valuable results might be obtained concerning the nutrition of patients if a similar, though larger, apparatus were placed in Bellevue Hospital. Before embarking on the undertaking, inquiry was made of Dr. Benedict if he did not desire to investigate this field by establishing a calorimeter in the Peter Bent Brigham Hospital in Boston. As the reply was in the negative, it appeared justifiable to seek money and opportunity for the accomplishment of this work.

Sufficient funds were obtained from the Russell Sage Institute of Pathology for a period of five years. The former arrangement between this institute and the City Hospital had just been terminated. A new arrangement was entered into with the trustees of Bellevue Hospital

7. Williams: Jour. Biol. Chem., 1912, xii, 317.

which enabled the institute to construct the first respiration calorimeter ever established in a hospital. Dr. Eugene F Du Bois was appointed medical director, and the whole undertaking has enjoyed the faithful service of chemists, mechanics and nurses who have contributed to its success. A factor of especial encouragement has been the personal interest in the undertaking manifested by the visiting physicians, Drs. W. Gilman Thompson, C. L. Dana and Warren Coleman. The last-named has taken part in the actual work of the institute.

It is also a pleasure to acknowledge with thanks many helpful suggestions made by Drs. Langworthy and Milner of Washington.

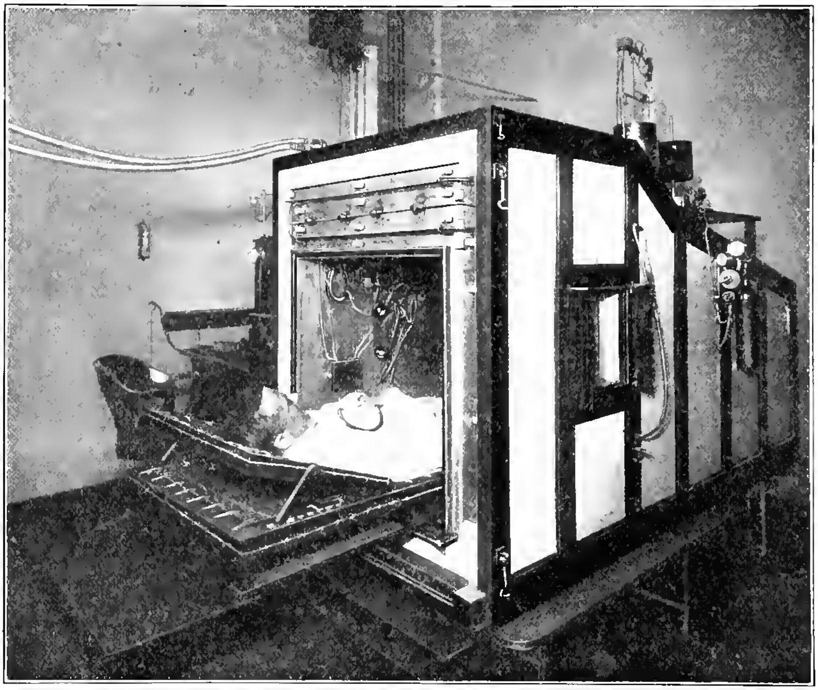

Fig. 1.—Respiration calorimeter with the patient half-way in. On his chest can be seen the tube of the Bowles stethoscope strapped over the heart. Coiled up on the wall is the rectal thermometer not yet inserted. Just below this is one of the units of the air thermometer and to the right is the telephone.

An Atwater-Rosa-Benedict respiration calorimeter, together with the instruments of precision applied to it by Williams, and certain new modifications which were the result of advice and experience, was established in Bellevue Hospital. The papers which follow are descriptive of the calorimeter (Fig. 1) and the results obtained with it. The patient lies quietly for three or four hours on a comfortable bed in the chamber of the apparatus, breathing the purest air, without the possi-

bility of harm. The long periods of the older respiration chambers and the nose- or mouth-pieces of the short-period apparatus are not disturbing factors. For the benefit of those who are interested in the work and who do not care to follow the details of the technical description of the apparatus, the following summary will suffice.

PRINCIPLE OF THE ATWATER-ROSA-BENEDICT RESPIRATION CALORIMETER

The apparatus is divided into two functional parts, one for measuring the gaseous exchange, the other for measuring the heat production of the subject. A schematic presentation is here given (Fig. 2).

The Gas Analysis.—The inner lining of the apparatus presents an air tight copper box having a capacity of 1,123 liters. One end of the box, through which the patient lying on the bed is admitted, may be closed with a glass plate by means of wax. The air within the box is purified by drawing it out of an opening in the box through a rubber tube and forcing it by means of a rotary blower through a system of *absorbers,* whence it returns again to the box by another rubber tube. It passes (see diagram) first through sulphuric acid (1), which removes the water, then through moist soda lime (2), which removes the carbon dioxid, and next through sulphuric acid (3), which absorbs the moisture taken from the soda lime. If the bottles be previously weighed, the gain in weight of 1 represents water absorbed, and the gain in weight of 2 plus 3 equals the carbon dioxid absorbed. By this method the water and carbon dioxid produced by a man are taken from the air, while oxygen within the chamber is being absorbed by the man himself. This causes a diminution in the volume of the contents of the box. In order to replace the oxygen used, oxygen is automatically fed into the system from an oxygen cylinder which may be weighed before and after the period. The automatic feeding of oxygen into the box is accomplished by means of a spirometer whose interior is connected with the interior of the calorimeter chamber. As the volume of the air in the box decreases, the spirometer falls until a certain point is reached, at which an electric contact releases a clamp, which allows oxygen from the oxygen cylinder to enter the box, causing the spirometer to rise, break its electric contact and clamp off the oxygen supply. So sensitive is the spirometer to the movement of the patient that a device called a "work adder" has been attached to it, which records the subject's movements.

At the beginning of an hourly period of experimentation an observer at the table calls "time." At this instant the rotary blower is stopped, the air current switched so as to pass through a new set of weighed absorbers and then the rotary blower is started again. At the word "time" an operator also turns a pet-cock which cuts off the respiratory chamber from the spirometer cylinder, which is then filled, always to a given point, with oxygen from the oxygen cylinder. The pet-cock is now opened and a freshly weighed oxygen cylinder is placed in the position of the other, which is removed. Repeating these procedures an hour later, one may determine by difference in weight the gain of water and carbon dioxid by the absorbers and the loss of oxygen by the cylinder. The figures are subject to corrections due to (1) gain or loss of water or carbon dioxid content in the box itself, during the period, which gain or loss must be added to or subtracted from the increase in weight of the absorber system. This gain or loss of water and carbon dioxid in the box also affects the volume of the air in the box and, therefore, the quantity of oxygen admitted, as do, in addition (2), a change in temperature within the box and (3) a change in barometric pressure. These corrections must be made in order to determine whether oxygen is to be added or subtracted from the quantity which has been furnished from the oxygen cylinder. The result

gives the quantity of oxygen which the man has absorbed. It is apparent that all the errors of determination fall on the oxygen, and yet the exactness of the method is witnessed by the close approximation in alcohol check experiments of the theoretical and actual values for oxygen consumed.

If a person in the calorimeter moves even the arm during the critical moments just before "time" is called, the increased local heating of the air may cause the spirometer to rise to a considerable height, of which the air

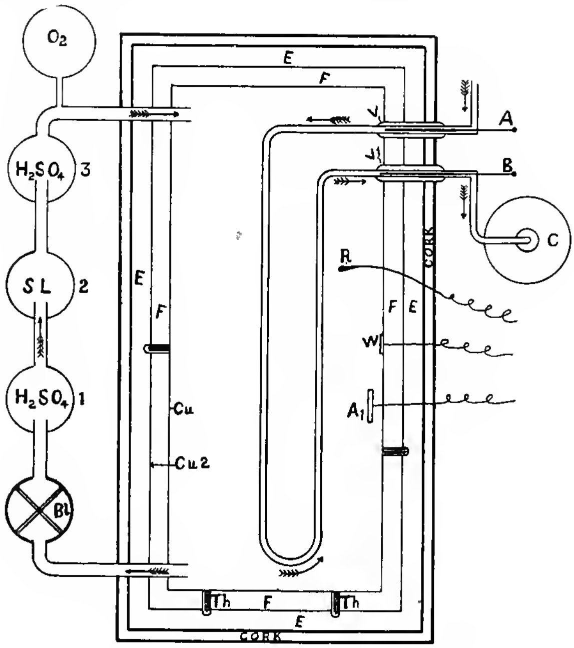

Fig. 2.—Schematic diagram of the Atwater-Rosa-Benedict respiration calorimeter.

Ventilating System:
- O_2, Oxygen introduced as consumed by subject.
- 3, H_2SO_4 to catch moisture given off by soda lime.
- 2. Soda lime to remove CO_2.
- 1, H_2SO_4 to remove moisture given off by patient.
- Bl., Blower to keep air in circulation.

Indirect Calorimetry:
- Increase in weight of H_2SO_4 (1) = water elimination of subject.
- Increase in weight of soda lime (2) + increase in weight of H_2SO_4 (3) = CO_2 elimination.
- Decrease in weight of oxygen tank = oxygen consumption of subject.

Heat-Absorbing System:
- A, Thermometer to record temperature of ingoing water.
- B, Thermometer to record temperature of outgoing water.
- V, Vacuum jacket.
- C, Tank for weighing water which has passed through calorimeter each hour.
- W, Thermometer for measuring temperature of wall.
- A1, Thermometer for measuring temperature of the air.
- R, Rectal thermometer for measuring temperature of subject.

Direct Calorimetry:
- Average difference of A and B $\times$ liters of water + (gm. water eliminated $\times$ 0.586) $\pm$ (change in temperature of wall $\times$ hydrothermal equivalent of box) $\pm$ (change of temperature of body $\times$ hydrothermal equivalent of body) = total calories produced.

Th, thermocouple; *Cu*, inner copper wall; *Cu_2*, outer copper wall; *E*, *F*, dead air spaces.

thermometers inside the box fail to make compensatory record, and the oxygen determination will be too low in that hour and too high in the next.

Analysis of the air in the interior of the chamber is made just before the beginning of each hour by passing ten liters of air from the box through three U-tubes containing, respectively, sulphuric acid, soda lime and sulphuric acid, then through a Bohr gas meter and back into the box again. This is called the "residual analysis."

Under the conditions present in the respiration apparatus, carbon dioxid is measured with the greatest ease and accuracy. Oxygen is also measured with accuracy if the person within the box lies perfectly quietly for ten minutes before the end of the period, whereas water production is the least accurate of all the determinations, on account of the varying hygroscopic condition of the walls, bedding and other surfaces within the closed spaces of the apparatus.

The Measurement of Heat Produced. — Roughly speaking, one-quarter of the heat eliminated by a man is present in the water vapor which is absorbed by the first sulphuric acid bottle on the absorber table. At 20 degrees C. 0.586 calories are contained as latent heat in 1 gm. of vaporized water.

The rest of the heat loss takes place by radiation and conduction. It is this heat which is measured by the calorimeter, itself. The mechanism of the calorimeter is essentially two-fold. In the first place, there is no heat loss through the walls of the apparatus, and, secondly, the heat produced by a man within is removed from the chamber by a current of cold water flowing through copper tubes suspended from the upper wall of the chamber. If the walls allowed no heat to pass, it is obvious that without the cooling effect of the water-pipes the temperature of the air in the box would soon attain the temperature of the human body instead of being about 23 C., at which it is usually held. The apparatus is therefore a constant-temperature, water-cooled calorimeter. It is evident that if no heat is allowed to pass through the walls of the calorimeter, then the heat produced within the chamber will be removed in the current of cold water flowing through the heat-absorbing pipes inside the chamber of the apparatus. If the temperatures of the ingoing and of the outgoing water are known and the quantity of water which has passed through the heat-absorber during an hour is measured, the quantity of heat carried away in the current of water can be accurately determined. For example, if the difference between the temperature of the ingoing and outgoing water is 2.50 degrees, and 20 liters of water have passed through the heat absorber in one hour, then 50 calories of heat have been carried away from the apparatus during the period. If the temperature of the walls within the apparatus has undergone a change this value is subject to corrections, but otherwise the total heat elimination of the person is meas-

ured by the 50 calories so determined plus the heat value of water vaporized during the hour.

To obtain an even flow of water through the heat-absorber the water is supplied from a constant-level tank placed above the calorimeter. To obtain ingoing water of an even temperature, Williams passed the previously ice-cooled water current through a Gouy temperature regulator and then through a current regulator designed by himself. These improvements allow the ingoing water to enter the calorimeter at a temperature which may not vary more than 0.02 C. during hours of experimentation and, for the first time, permitted the exact measurement of small quantities of heat in this type of apparatus. The temperatures of the ingoing and outgoing water are taken every four minutes by electrical resistance thermometers and are read in connection with a galvanometer and Kohlrausch bridge on an observer's table. The quantity of the water-flow is determined by weighing; the water is diverted at the call of "time," so that the exact quantity for the hour is collected in a previously weighed receptacle.

Having learned how the heat produced within the apparatus is carried away, the problem of how to prevent loss of heat through the walls of the chamber remains to be discussed. This was accomplished through a device introduced by Rosa. The calorimeter is constructed of three walls, an inner copper wall which has already been described as the lining of the respiration chamber, an outer copper wall separated from the inner wall by a space of dead air, and an insulating wall (made of two layers of "compo-board," the space between them being filled with cork), which insulating wall is separated from the outer copper wall by a second space containing dead air. It is obvious that if the inner and outer copper walls of the calorimeter have the same temperature there will be no exchange of heat between them. Therefore, to prevent a gain or loss of heat by the inner wall, it is necessary to maintain the outer wall always at exactly the same temperature as the inner wall, under which circumstances the latter cannot gain or lose heat to its neighbor.

In order to detect differences in temperature between the outer and inner walls Rosa arranged thermo-couples in series between the two walls. In this fashion the top, sides and bottom of the box are successively tested every four minutes by an operator at the observer's table to determine whether there is any difference in temperature between the outer and inner walls. If the outer wall is found to have a different temperature from the inner wall, its temperature is brought to that of the inner wall by the following device. A cooling current of water runs through pipes between the insulating and outer copper wall, and in this same space, along the line of the pipes, run "Therlo" resistance

wires carrying an electric current for the warming of this inter-space (Fig. 1). By varying the intensity of the electric currents which severally supply the spaces to top, sides and bottom, the temperature of these spaces can be so controlled as to heat or cool the outer copper wall and maintain it at exactly the same temperature as the inner copper wall. This is the effective system which prevents a loss or gain of heat through the wall of the calorimeter.

Resistance thermometers are attached to the inner walls of the calorimeter, and if the temperature of the walls rises or falls between the beginning and end of the experiment, a correction must be made. It has been found that 19 calories are absorbed by the Sage calorimeter when the inner wall rises 1 degree. Conversely, 19 calories are given up by a fall of 1 degree. This is the *hydrothermal equivalent* of the box.

SCHEME OF EMPLOYMENT OF OBSERVERS IN A CALORIMETER EXPERIMENT

Period of Observation	Observer 1, at Electrical Control Table	Observer 2, in Charge of Experiment	Observer 3, Calculator
Eight minutes before	Brings wall into exact thermal equilibrium	Signals subject to lie absolutely quiet.	Starts passing first 10 L. sample of residual air through U tubes.
Five minutes before	....	Starts kymograph record of movements of spirometer	....
Four minutes before	....	....	Finishes first and starts second residual
One-half minute before	Takes final reading of air, wall and rectal temperature	Sets barometer	Finishes second residual
At "Time"	Presses button which diverts stream of water from weighing tank	Shuts spirometer off from box. Fills to standard level from oxygen tank.	Stops ventilating current of air. Turns valve to pass air through newly weighed absorbers. Starts ventilating current.
Immediately after "Time"	Starts taking readings every four minutes of ingoing and outgoing water, of air, walls, rectal and surface thermometers. Reads and adjusts temperature of top, sides and bottom of calorimeter, of the ingoing air and water every four minutes, or oftener if necessary.	Records and sets work-adder. Signals to subject that he may move. Weighs oxygen tank and connects with box again. Weighs sulphuric and soda lime bottles. Connects them up again and tests for leaks. During remainder of hour counts pulse, inspects valves for leaks, adjusts temperature of room, watches subject, etc.	Weighs water tank which has received all the water from the heat absorber during the past hour. Diverts stream of water to this tank again. Records barometer. Weighs residual. Calculates results of the hour just finished.

The temperature of the air entering the box from the absorbing table is always heated to exactly the same temperature as the air leaving the box.

Finally, an electric resistance thermometer inserted 10 or 12 cm. into the rectum of the person in the calorimeter gives information regarding the retention or loss of heat in his organism. The specific heat of a man is assumed to be 0.83, that is to say, 0.83 calory raises 1 kilogram 1 degree. If, therefore, the body temperature of a man weighing 70 kg. rises or falls 1 degree, the quantity of heat lost or

gained by the body will be 70 $\times$ 0.83 or 58.1 calories. This is on the assumption that the rise of body temperature is everywhere the same as takes place in the rectum, a supposition which, unfortunately, is not always true.

The accompanying scheme (Table 1) gives the details regarding the employment of the three individuals who conduct a calorimeter experiment.

It may be added that special care has been taken to make the appearance of the calorimeter attractive to the eye, and that the spirit of the small ward in connection with the calorimeter work has been such that the patients have considered themselves especially fortunate when chosen for the diversion offered by a morning's occupancy of the apparatus.

CONCLUSION

The story of the Atwater-Rosa-Benedict calorimeter has been told here for the first time in brief, comprehensive, perhaps one might say semipopular language. The Williams calorimeter has shown the influence of many simple foodstuffs which were given to dogs in health and in induced disease. The Sage calorimeter reports "of the disturbances that Nature works and of her cures," without having, as concerns the sick human being, at any time, in the slightest degree, affected any patient to his disadvantage, but rather having yielded information regarding his condition which has been beneficial in his subsequent treatment.

It seems appropriate to recall the words with which Pettenkofer and Voit closed their communication regarding diabetes in the year 1867:

> Even as anatomy has been separated from physiology, so from pathological anatomy pathological physiology will arise. Only thus will we be able to obtain a more exact knowledge of the character of disease than we now possess. Able pathologists have constantly sought to open up this field. It will gratify us if this work of ours which for the first time presents a complete picture of metabolism in disease shall inspire others to devote their abilities in this direction.

CLINICAL CALORIMETRY

SECOND PAPER

THE RESPIRATION CALORIMETER OF THE RUSSELL SAGE INSTITUTE OF PATHOLOGY IN BELLEVUE HOSPITAL *

J. A. RICHE AND G. F. SODERSTROM

NEW YORK

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10. Limits of error in measuring heat, carbon dioxid and oxygen.
11. Determination of water elimination.
12. Adaptability of calorimeter to varying conditions.
13. Summary and conclusions.

During the short time in which the Sage calorimeter has been in operation there have been several requests for the technical details of the construction of the apparatus. It has therefore seemed advisable to publish a brief article for those interested in calorimeters. A complete description of the Atwater-Rosa-Benedict type of apparatus will be found in the monograph by Benedict and Carpenter.[1] A number of valuable improvements are added in the shorter article by Williams.[2] The earlier publications of Atwater and Rosa[3] and Atwater and Benedict[4] describe an apparatus fundamentally the same as that now employed, but for a complete understanding of the modern calorimeter it is necessary to consult the works of Benedict and Carpenter and

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Benedict and Carpenter: Respiration Calorimeters for Studying the Respiratory Exchange and Energy Transformations of Man, Carnegie Institution of Washington, 1910, Pub. 123.

2. Williams, H. B.: Animal Calorimetry, First Paper, A Small Respiration Calorimeter, Jour. Biol. Chem., 1912, xii, 317.

3. Atwater and Rosa: Description of a New Respiration Calorimeter, U. S. Dept. Agriculture, 1899, Bull. 63.

4. Atwater and Benedict: A Respiration Calorimeter with Appliances for the Direct Determination of Oxygen, Carnegie Institution of Washington, 1905, Pub. 42.

Williams. The description by Langworthy and Milner[5] of their ingenious automatic calorimeter should also be consulted.

The Sage calorimeter resembles Benedict's bed calorimeter, but differs in a few details. On the recommendation of Dr. Langworthy and Mr. Milner of the Department of Agriculture the outside insulation was made of pressed cork and "Compo Board." The electrical resistance thermometers for the ingoing and outgoing water were also adopted on their advice. The gas wash bottles, water heating resistance and current regulator, water coil and several other improvements were copies of those used by Williams. The soda-lime bottles and spirometer resembled those described by Benedict[6] in connection with his small apparatus.

THE CALORIMETER ROOM

The small metabolism ward to be described is situated at the southwest corner of the new medical pavilion of Bellevue Hospital. To the north of this is a hall, now converted into a diet kitchen, which leads into the calorimeter room, formerly a small ward for convalescents. The room itself (Fig. 3) is about 5 meters square and 5 meters high. On the west side, opening on a covered balcony, is a large window in front of which stand a thermostat-controlled radiator and a "Simplex" electric heater. These are enclosed in a window box in such a manner, that by means of a blower, fresh air can be drawn in through the window, driven over the heaters and out into the room. Unfortunately, the daylight is not strong and needs to be supplemented by two powerful tungsten lamps.

In the center of the room stands the calorimeter, at the side of which is the observer's platform, raised a short distance above the floor to permit the passage of the numerous water pipes and electrical conduits. On the east side of the room is the panel box where the heavy feed wires are led up from the basement. Next to this panel box are the storage batteries with charging board used in electric checks. On the south side of the room, where the door is situated, enough space has been left to wheel a stretcher with a patient to the front of the calorimeter. By making careful use of every inch a great deal of apparatus has been placed in a small room without crowding those who work there.

THE FRAME

As the photographs show, the calorimeter was made high enough at the head to allow the subject to sit upright. This increases the

5. Langworthy and Milner: Year Book U. S. Dept. Agriculture, 1910, p. 307; ibid., 1911, p. 491.

6. Benedict, F. G.: Ein Universalrespirationsapparat, Deutsch. Arch. f. klin. Med., 1912, cvii, 156.

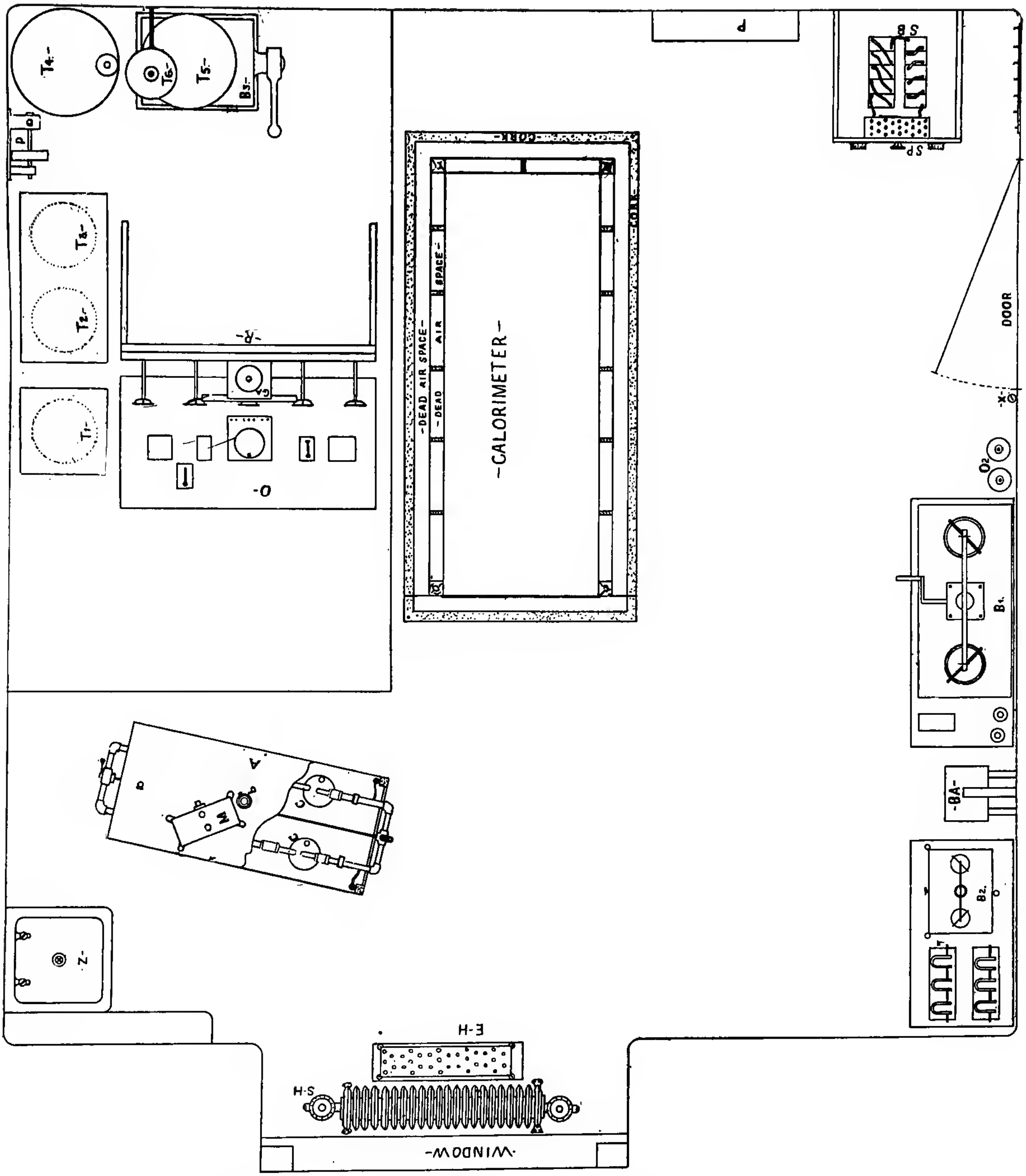

Fig. 3.—The calorimeter room. A, Absorber table. M. Bohr meter. b, Drying tower for air sample drawn through meter. CC, Williams bottles containing sulphuric acid. SH, Steam heater. EH, Electric heater. Z, Sink. O, Observer's table. Ga, Galvanometer. R, Rheostat board. T_1, Gouy regulator tank. T_2, Ice tank for cooling water running through absorber in calorimeter. T_3, Ice tank for water to cool outer copper wall. T_4, Large supply tank. T_5, Tank on platform balance (B_3) for weighing water. T_6, Small tank to hold water from absorber while T_5 is being weighed. p, Pump to lift water from T_4, to constant-level tank near the ceiling. P, Panel box. SB, Edison storage batteries. SP, Charging panel. x, Pyrene fire extinguisher. O_2, Oxygen tanks. B_1, Balance for sulphuric bottles, etc. Ba, Barometer. B_2, Balance for U-tubes.

volume of contained air and magnifies certain errors, but makes the box much more comfortable and apparently gives better results than if the quarters were cramped. The frame (Fig. 4) was made of wood, as previous experience with the small calorimeter in Cornell had shown that the mass of angle iron between the metal walls made the box very sluggish in responding to temperature changes. To prevent warping, which would be disastrous, the best quality white pattern pine was used and the frame allowed to stand for several months before it was shellacked. The outside timbers were 6.35 by 6.35 cm. square and the braces 6.35 by 1.9 cm. All joints were glued and dowelled. The braces were spaced 30.48 cm. apart to give rigidity to the copper walls which are attached to the wood in many places.

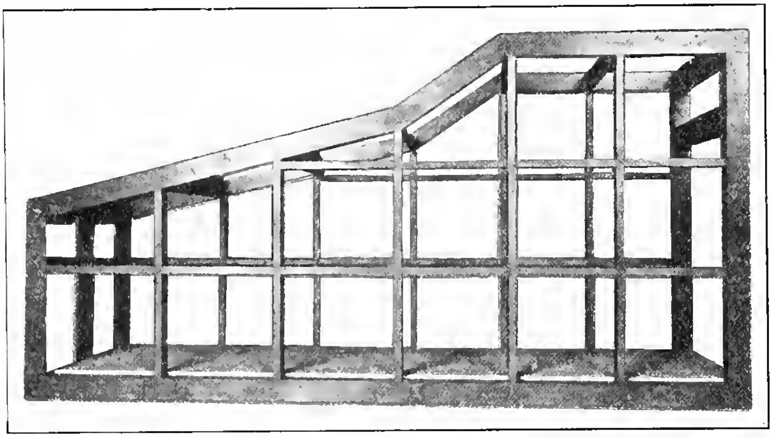

Fig. 4.—Wooden frame of calorimeter with asbestos board as floor.

COPPER WALLS

The inner copper wall (Fig. 5) forms an air-tight box 198.18 cm. long, 76.2 cm. wide, 91.4 cm. high at one end and 45.7 cm. at the other, with a capacity of 1,123 liters. At the head is an opening to serve as a door and on one side an opening for a window.

The wall is made of "16-ounce" sheet copper, tinned on the inside. It is fastened to the inner side of the wooden frame by means of brass angles soldered to the copper and screwed to the wood. The bottom rests on a long slab of asbetos board 9.5 mm. thick.

The outer copper wall (Fig. 6) which is screwed directly on the outer side of the wooden frame, does not come in metallic contact with the inner wall at any place except the rim around the large opening at the head of the box. This outer wall is made of "14-ounce" copper tinned on the outside, and while the joints are soldered they are not necessarily air-tight.

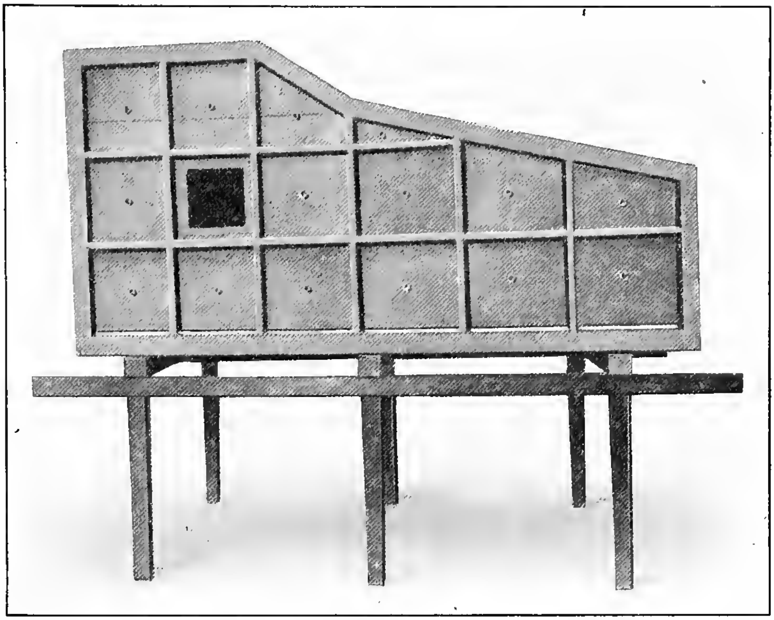

Fig. 5.—Inner copper box with brass thimbles for thermopiles.

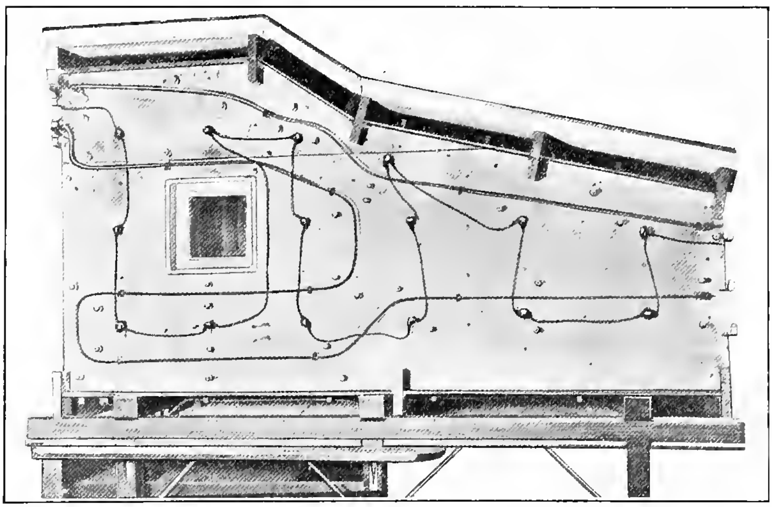

Fig. 6.—Outer copper box with leads connecting thermopiles, pipes for cold water and porcelain insulators for resistance wires. The wires themselves are not shown in the photograph. The top and bottom of the wooden box are in position.

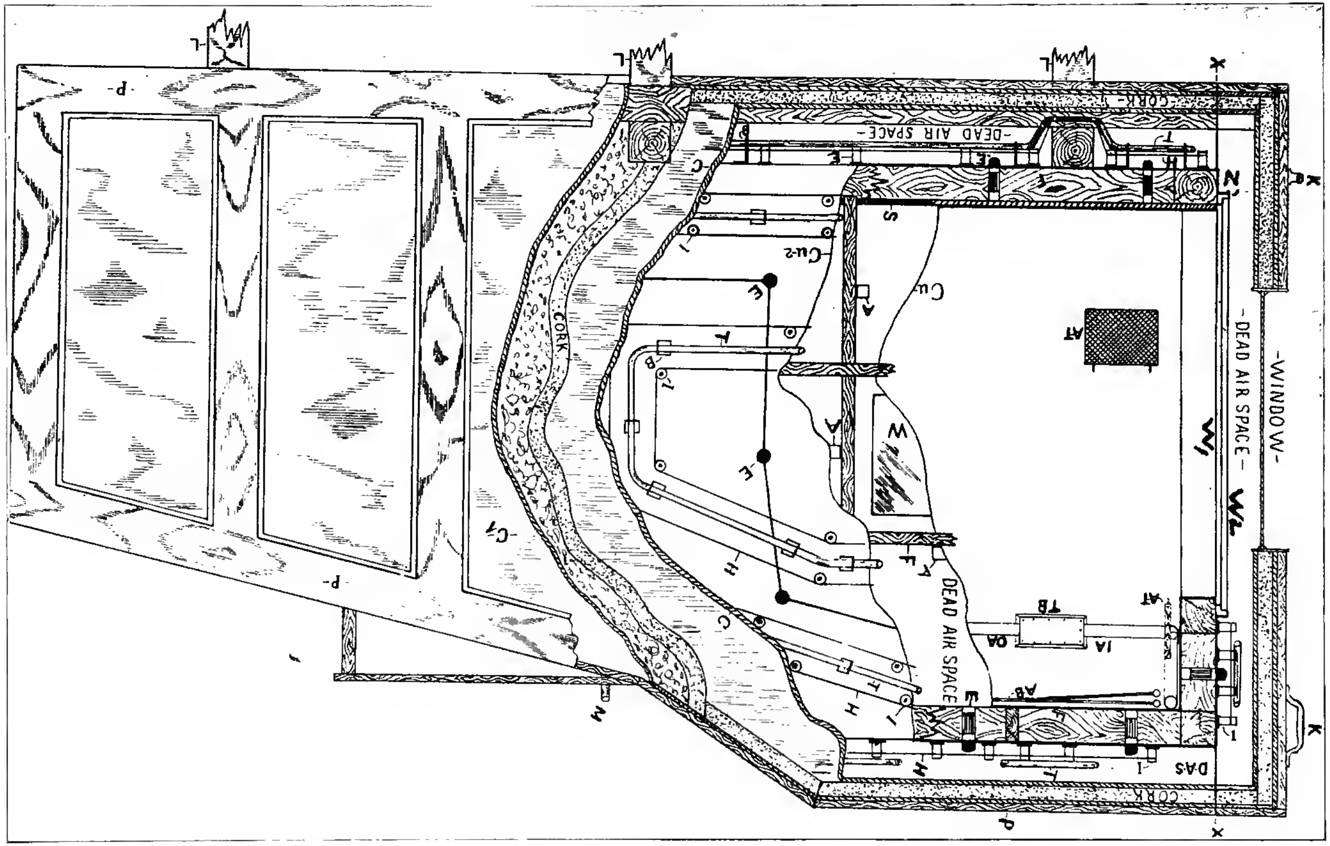

Fig. 7.—Sectional view of the calorimeter. AA, Brass angles fastening inner copper wall to wooden frame. AT, Air thermometer. AB, Heat absorber pipes. BB, Brass angles supporting cold water pipes on the outer copper wall. C, Inner layer of "Compo Board." C_1 Outer layer "Compo Board." Cu, Inner copper wall. Cu2, Outer copper wall. DAS, Dead air space. EE, Thermopiles. F, Wooden frame. H, Resistance wire. I, Porcelain insulators. IA, Ingoing air pipe. K, Handles of wooden panel at head of box removed at line X - X. L, Wooden legs of calorimeter. M, Pipe leading from interior of box to spirometer. N, Copper frame in which are placed glass plates W_1 and W_2. OA, Outgoing air pipe. P, Wooden supports for "Compo Board." S, Asbestos board under floor of calorimeter. TT, Cold water pipe. W, small window.

The braces of the wooden frame divide the dead air space between the walls into compartments about 30.48 cm. square and 6.35 cm. thick. In the center of each compartment is placed a thermopile with four thermocouples in thermal but not in electrical contact with each copper wall. The inner end of this thermopile fits in a brass thimble 25.4 mm. deep soldered to the outer side of the inner wall. The outer end (with its four thermocouples) fits in a brass tube which passes through the outer wall and is closed off from the outside air by P. B. Compound and electric tape.

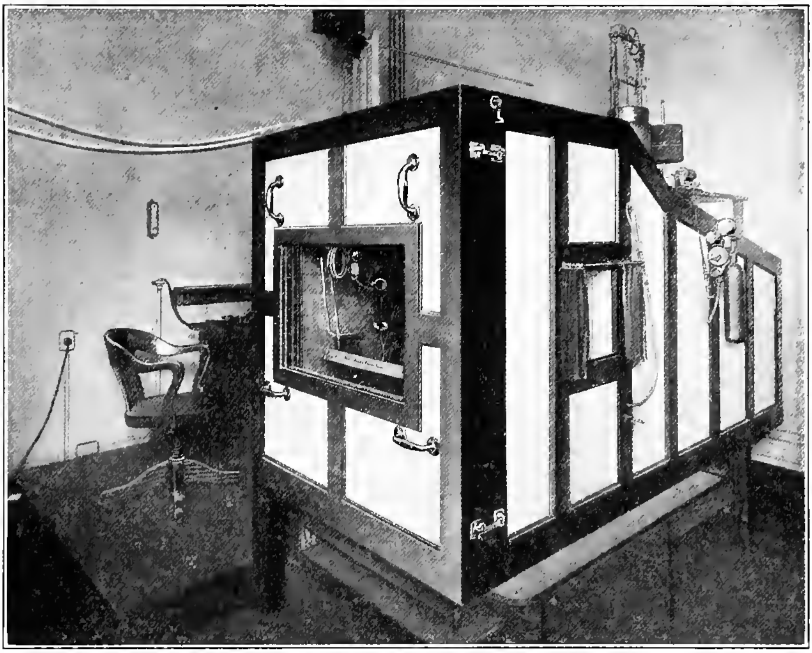

Fig. 8.—Calorimeter with front closed.

In Figure 13 the large opening at the head of the box, measuring 76 by 70 cm., is closed by two glass plates 7.5 mm. thick, each sealed after the subject has entered the calorimeter by means of a mixture of 5 parts bees-wax and 1½ parts Venice turpentine. The small window in Figure 6 is permanently closed by glass plates fastened to the copper walls. There are numerous pipes and electric cables entering the box as will be described later.

On the surface of the outer copper wall are attached the wires connecting the thermopiles. The pipes for cold water are swung on brass angles attached to this surface and the enameled "Therlo" resistance wire is bound on insulators to the same surface, very much as described by Benedict and Carpenter.

INSULATING WALL

Completely surrounding the outer copper wall and separated from it by a space of 7 cm. is the thick wall intended to protect the calorimeter from fluctuations in the room temperature. This is constructed of a layer of pressed cork 2.54 cm. thick, between two layers of "Compo Board," a patented building material made of strips of wood glued between layers of stout paper. This is supported by a framework of white-wood, making panels which are light, yet very effective as heat insulators. The head of the wooden box is provided with a glass window and furnished with handles so that it can be easily removed when the experiment is over and placed on a small shelf on the right of the calorimeter. The frame of this outer box is stained to resemble oak, and the "Compo Board" panels are painted with white enamel. Every effort has been made to make the room and the calorimeter pleasing to the eye, with the result that patients are attracted by the beauty of the apparatus rather than by its resemblance to a coffin.

THE ABSORBER TABLE

The absorber table is so arranged that the air current is switched from one set of absorbers to the other by means of a three-way valve. This works satisfactorily and is much quicker than the old style seat-valves. The sulphuric bottles are larger models of the form described by Williams and hold about 1¼ liters of acid, which will remove every trace of moisture until more than 100 grams has been absorbed. The soda-lime bottles resemble those devised by Benedict,[6] except for a modification of the tube which carries the entering air. This is divided in such a manner that the soda-lime can be packed about a brass pipe, the lower end of which is perforated and the upper end of which reaches almost to the top of the bottle, where it fits snugly in an elbow attached to the stopper. The Crowell blower is the same as the ones used by Williams and Benedict, but a safety device has been attached to prevent accidental reversal of the blower which would have disastrous effects. The two small bicarbonate cans next to the last sulphuric bottle did not remove entirely the acid vapors and it was necessary to place a long cylinder in the vertical pipe which carries the air from the absorber table. This contains about 340 grams of bicarbonate of soda packed between layers of cotton and catches all traces of acid fumes.

The air enters the box in a pipe which ends in a single opening directed just above the subject's head and leaves through a number of small openings in a pipe which runs across the foot of the box. A small electric fan at the lower end of the calorimeter keeps the air well stirred.

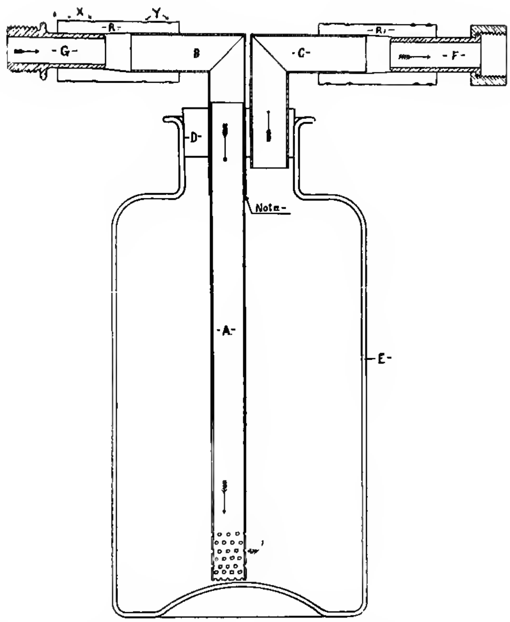

Fig. 9.—Modified soda-lime bottle. A, Brass tube with perforated bottom and top which fits in brass elbow, B. The bottle is filled with A in position and the rubber stopper D with elbows B and C is then forced into neck of bottle. G and F, Brass couplings. R and R_1, heavy rubber tubing. X and Y, Binding wires.

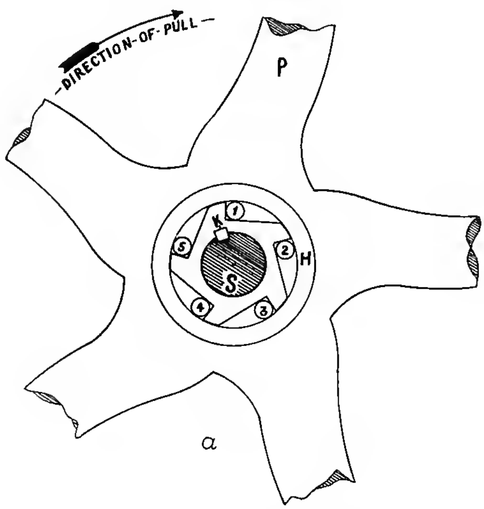

Fig. 10.—Safety device to prevent blower from being reversed. P, Pulley for belt to motor. S, Shaft of blower. H, Hub of wheel. K, Key 1, 2, 3, 4, 5, hardened steel rollers which engage when pulley is running in right direction, but disengage when pulley starts in opposite direction.

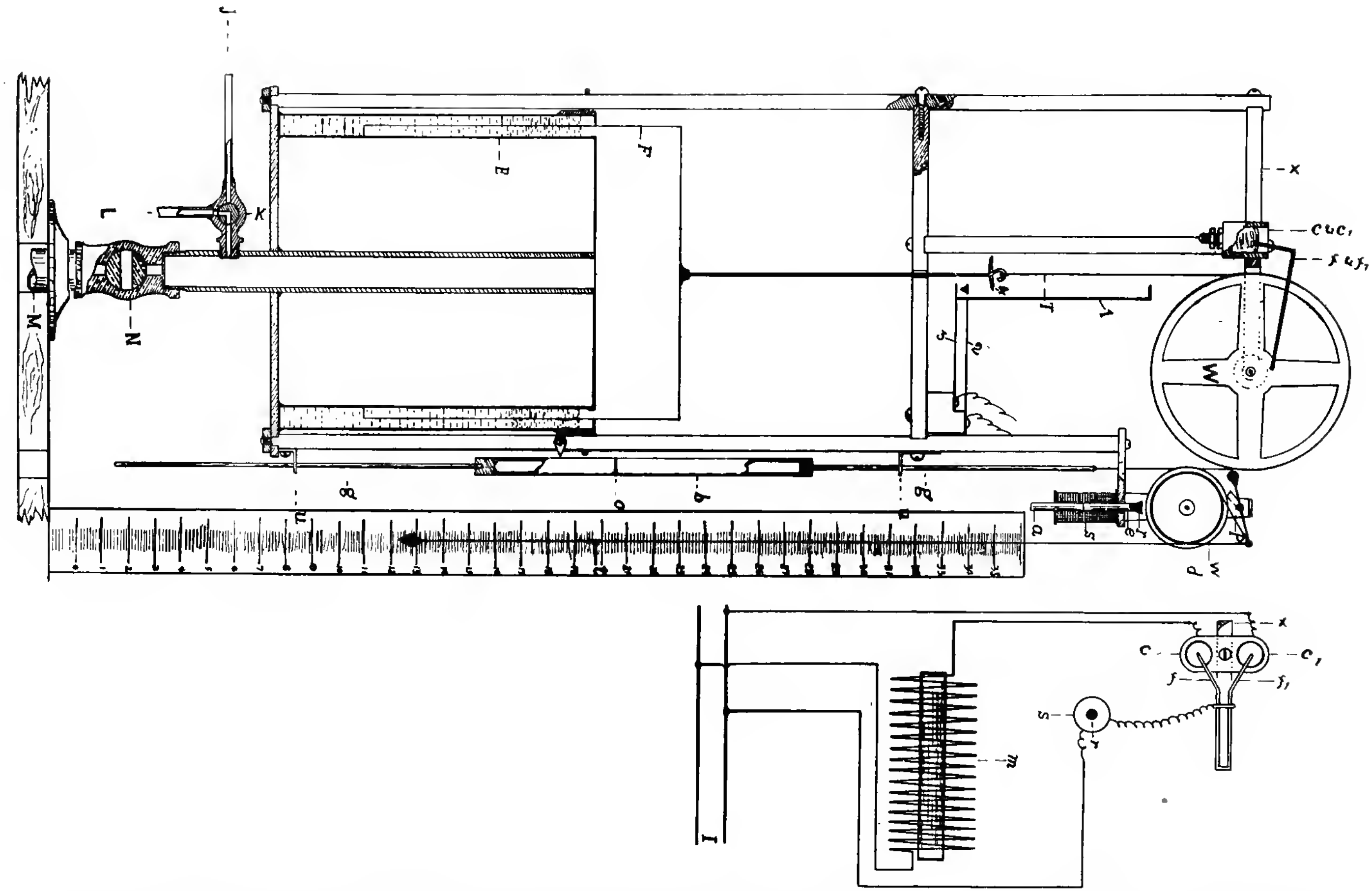

Fig. 11.—Spirometer and Work-Adder. M, Pipe from calorimeter to spirometer. N, two-way valve. J. Small pipe to ingoing air pipe. L, Oxygen inlet. K, Three-way valve arranged to admit oxygen into ingoing air pipe or into spirometer. E, Spirometer tank filled with water. F, Spirometer bell of light copper. T, String supporting bell. W, Wheel supporting bell. b, Counterpoise filled with mercury. gg, Guiding rod fitting loosely in uu. o, Mark on counterpoise. The spirometer is filled at the end of each period until this mark is opposite the pointer. w, Work-adder with toothed edge and cam. d, Drum on which is wound the thread t. P, Small lever with eye through which thread passes. When the thread is pulled downward the cam is lifted. s, Solenoid. r, e, a, Plunger which is raised by solenoid, pressing against edge of work-adder while the spirometer bell is being raised by the admission of oxygen. r, Soft rubber; e, hard rubber; a, iron. x, brass support. c and c_1, mercury cups into which dip f and f_1 when the spirometer bell sinks, making contacts which raise plunger and energize magnet m, thus admitting oxygen. I, Low voltage current corresponding to I, of Fig. 15. 1, 2, 3, 4, Automatic alarm which rings a bell whenever spirometer rises dangerously high or sinks too low. 4, A button on the rod supporting spirometer bell makes contact between 2 and 3 either by raising hook 1, connected with 3, or by depressing the small triangular knob connected with 2.

The spirometer on the top of the calorimeter resembles Benedict's[6] except that it is provided with a work-adder to record movement of the patient and not the total ventilation of the lungs. The bell is made of very light copper, is suspended in water and is carefully counterpoised. The counterpoise is provided with a writing point which records on a smoked paper the movements of the drum. To the wheel at the top is attached a brass arm with two points which dip into mercury cups set at slightly different levels whenever the spirometer bell

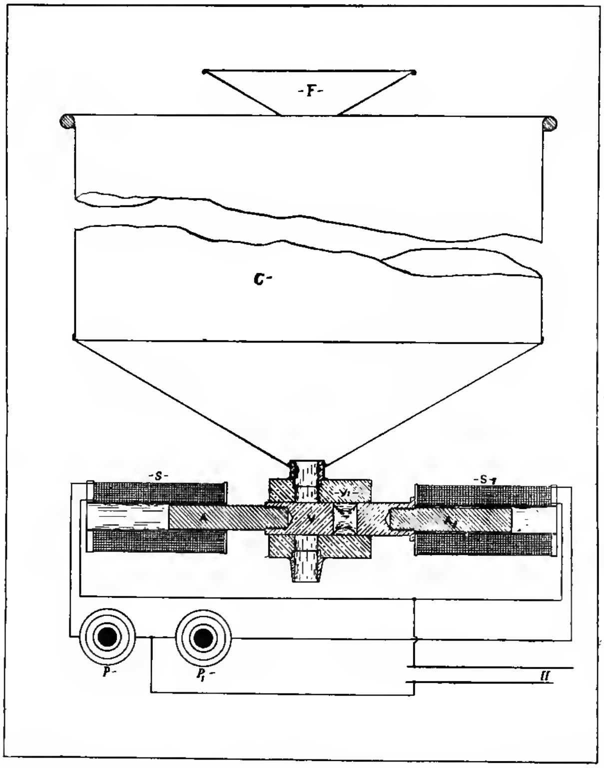

Fig. 12.—Electrical device for shutting and opening valve P. P_1. Push buttons controlling solenoids S and S_1. A and A_1 iron cores attached to brass rod V. Valve is shown closed. When current is passed through S the Rod V will be drawn to the left and the narrow portion seen just under V_1 will come opposite the pipe leading from receiving can G.

sinks below a certain mark. One of these cups operates a magnet which opens the attachment that automatically admits the oxygen. This keeps the spirometer within about one centimeter of the same level unless the subject moves and suddenly heats the air locally. It is remarkable how promptly the spirometer rises when the person within the box makes even a slight movement of a hand or leg. In fact, it makes so delicate a

movement recorder that a Porter work-adder has been attached in such a manner that the downward movement of the counterpoise winds up a thread and the total amount of thread so wound represents the total work done by the patient during that particular period. By standardizing various movements of the body such as turning over or lifting the arm it is possible to gain a fairly accurate idea of the amount of mus-

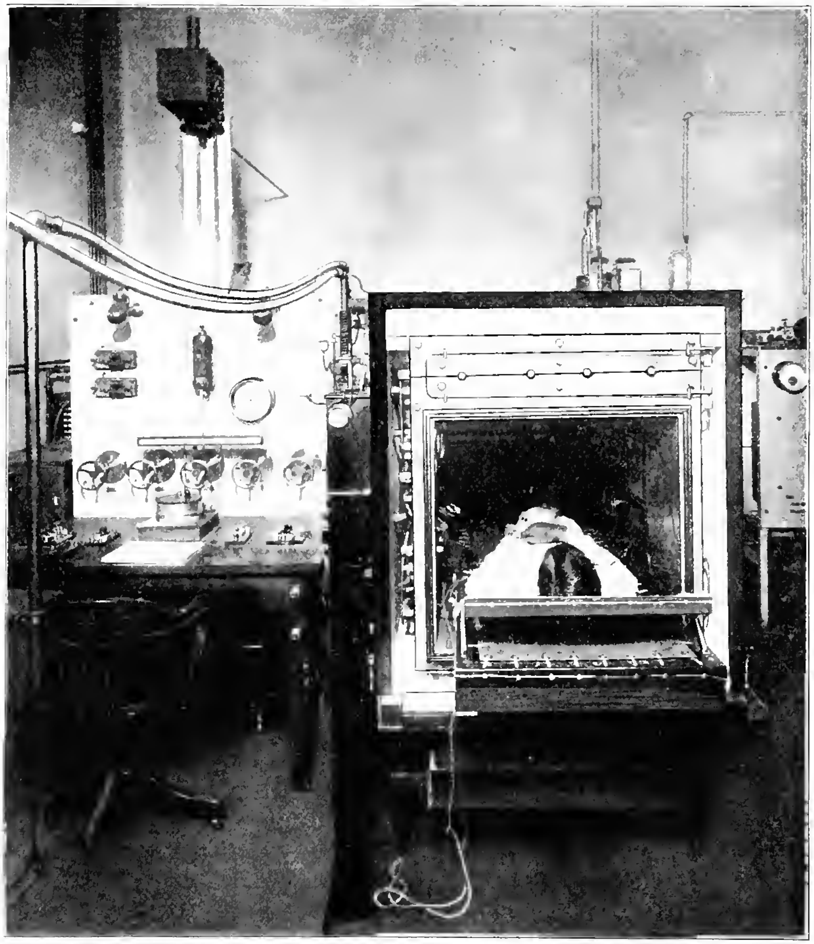

Fig. 13.—View of open calorimeter. Patient on canvas bed partly in the chamber. On the left can be seen the observer's table and the rheostat board with the galvanometer. The rubber pipes for outgoing and ingoing air lead to the absorber table, a corner of which can be seen on the extreme left. In the background on the right are the storage batteries and charging panel.

cular movement and express it in centimeters of thread, thus obviating the necessity of printing long graphic records. In order to prevent the work-adder from winding up thread while the oxygen is being admitted,

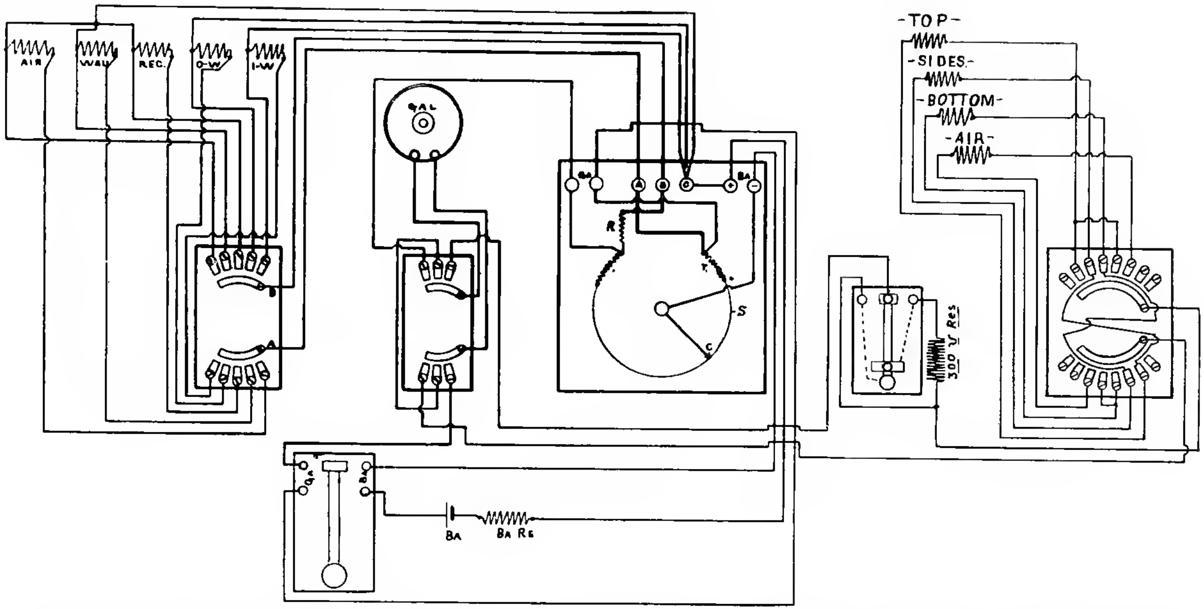

Fig. 14.—Wiring diagram of observer's table. In the center is the Kohlrausch bridge, to the right a tapping key with an arrangement for throwing in 300 ohms resistance when needed. This key is used in reading the thermopiles connected with the switch on the right. To the left of the bridge is a switch for connecting either thermopiles or resistance thermometers with the galvanometer. On the extreme left is the switch for the air, wall, rectal, ingoing and outgoing water thermometers, each of which contains 100 ohms. Since this diagram was made two additional thermometers for surface temperature have been added. In the front of the table is a tapping key.

a solenoid is connected with the second mercury cup into which the brass arm on the wheel dips. This solenoid operates a small plunger which holds the work-adder while the magnet opens the oxygen valve and also maintains its hold for the instant after the oxygen has been shut off, since the spirometer rises somewhat slowly after the admission of oxygen. This solenoid lag, which corresponds to the spirometer lag, is secured by having the second mercury cup filled slightly more than the cup which controls the oxygen magnet.

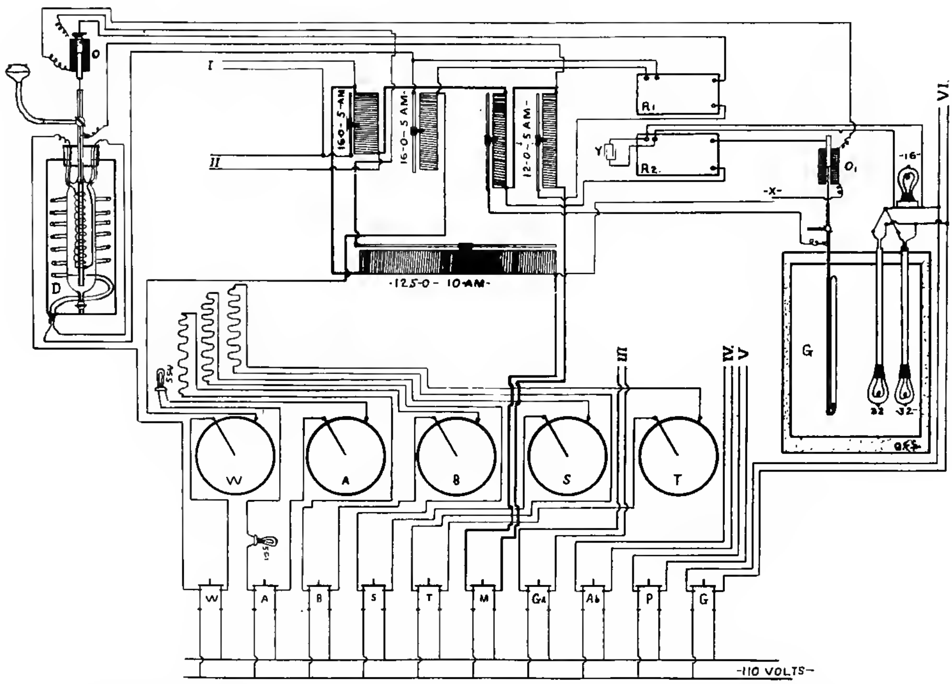

Fig. 15.—Wiring diagram of rheostat board. W, Switch and rheostat to control temperature of ingoing water in water heating resistance, D. A, Ingoing air. B, Bottom of calorimeter. S, Sides. T, Top. Ga, Galvanometer lamp. Ab, Motor on absorber table. P, Motor for pump. G, Lamps in Gouy regulator. M, Miscellaneous parts connected with tube rheostats. O, O_1, Solenoid agitators lifting and dropping platinum contacts with mercury in Gouy and current regulator as the contact is made and broken mechanically at x. R_1, Relay for current regulator. R_2, Relay to control heating of lamps in Gouy.

The heat-absorbing system is the same as that described by Williams, the Gouy regulator and Williams' water heating resistance and current regulator giving very satisfactory results. The water coil suspended from the roof of the calorimeter has, however, been wound with brass "jack chain" to increase its absorbing surface. From this coil the water runs to the weighing tank on the platform of a "silk scale"

which is sensitive within 10 grams. The flow of water was formerly cut off by hand at the end of each period, but this is now done by a pair of solenoids controlled by the operator at the observer's table, thus reducing the staff by one man. The stream of water runs constantly through a can which has the capacity of 10 liters, and is provided at its lowest point with a valve that is opened and shut by the pair of solenoids above mentioned. At the end of a period the valve is shut and the water collects in the can while the tank is being weighed. After the weighing is finished the valve is opened and the water runs once more into the tank.

RHEOSTAT BOARD AND OBSERVER'S TABLE

The marble rheostat board and the observer's table resemble closely those described by Williams. This rheostat board, the panel box, charging panel for the storage batteries, conduits, wires, etc., were installed by the Electric Construction Supply Company after specifications kindly drawn up for us by the Department of Water Supply, Gas and Electricity of New York City. Directly above the rheostat board is mounted a galvanometer of the d'Arsonval type, provided with prisms so that the ascending ray of light from the lamp below is reflected from the mirror of the galvanometer downward to a scale just above the table. (Siemans and Halske.) This vertical mounting with scale that can be read by daylight saves a great deal of room. The galvanometer is braced securely and does not vibrate. To protect it from the dust it is covered with a thin copper hood. The resistance of the moving system is 45 ohms and there is a ballast resistance of 200 ohms in series, which, however, is not used.

Most of the precision switches used were furnished by Siemans and Halske, Catalogue Number 17327. One of similar design was made in our own shop. A new device which has given great satisfaction has been introduced into the switch connecting thermopiles with galvanometer. At the start of the experiment, or at any other time when the temperature differences between outer and inner walls are large, a resistance of 300 ohms is kept in series. As soon as the calorimeter is in balance a button on the switch is turned and the resistance short-circuited, making the adiabatic control extremely delicate. The Kohlrausch bridge provided by the Leeds and Northrup Company of Philadelphia is similar to the one described by Williams. The 60-step rheostat for controlling the temperature of the ingoing water and the four 45-step rheostats controlling that of the ingoing air, bottom, sides and top of the outer copper wall, were made by the Simplex Heater Company of Cambridge, Mass. They are mounted on the back of the board with their handles projecting through the board to the observer's

table. Just above them on the back of the marble slab are the five tube rheostats (Siemans and Halske) used to cut down the current to various small pieces of apparatus. On the front of the board are the two relays, one for the Williams water heating resistance and current regulator and the other for the Gouy regulator.

The thermopiles between outer and inner copper walls are arranged in three groups, thirty-two on the top, thirty on the sides and twelve on the bottom, the area covered by each group being warmed by a strand of enamelled "Therlo Wire," No. 24 B & S gauge, whose temperature is controlled by one of the step rheostats.

One thermopile is arranged with one end in the outgoing air current and the other in the ingoing air. The temperature of the latter is adjusted to that of the former by means of a step rheostat and two 55 volt lamps. A similar rheostat controls the temperature of the ingoing water by means of the water heating resistance.

THERMOMETERS

All thermometers contain 100 ohms resistance in nickel or platinum wire and are made on the three-lead system, being read on the same galvanometer used for the thermopiles. The water thermometers made by Leeds and Northrup are similar to those constructed by them for the automatic calorimeter of the Department of Agriculture. They are described in the Leeds and Northrup catalogue (Bulletin 811) and also by Dickinson and Mueller[7] of the United States Bureau of Standards. In our hands they have been most satisfactory, since they are more accurate, easier to calibrate, and easier to read than mercurials. The Leeds and Northrup air thermometer, similar to that used by Williams, is in eight divisions scattered over the inside of the box so as to give the average temperature of the air. They are connected in series by copper wire covered with rubber and a casing of lead, a combination made especially for us which has given good service. The wall thermometer consisting of eight divisions in series was made in this laboratory. Each division was made of No. 38 double silk covered nickel wire wound around a strip of mica and held 2 or 3 mm. from the inside of the inner copper wall. Over this was soldered a shallow copper box so that the resistance wire would lie in a small air space completely surrounded by metal at the temperature of the wall.

The rectal thermometer is of a new design made to respond more rapidly to changes in the temperature than the old type in which the resistance wire was surrounded by a jacket of dead air. The nickel wire with its double silk covering is wound on a small piece of ivory

7. Dickinson and Mueller: New Calorimetric Resistance Thermometers, Bull. Bureau Standards, 1913, ix, 483.

and dipped in a round ended silver tube filled with molten Wood's fusible alloy at a temperature of 96 C. This is solidified by dipping in water, thus forming direct metallic contact between the outside of the silver tube and the insulated wire. The leads from the thermometer are enclosed in a soft rubber tube. The surface thermometers are made of flat circular buttons of ivory 25 mm. in diameter and 5 mm. thick. One side of the button is hollowed out to a depth of 3 mm., the edges being filleted. On the bottom of this depression is wound concentrically the resistance wire. On this is poured the molten Wood's metal until it is flush with the original level of the ivory. Two of these units are used in series in each of the two surface thermometers. They are strapped to the skin with adhesive plaster and covered with a pad of cotton wool about 20 cm. in diameter and 4 cm. thick, this also being held in place with adhesive plaster.

The air thermometers were calibrated by the makers and the wall thermometers made to contain exactly the same resistance. Since they are used only to denote relative changes in temperature, a more exact calibration is not necessary. The rectal, surface and water thermometers are standardized several times a year by means of very accurate mercurials, certified by the Physikalische Technische Reichsanstalt. When calibrating them one notices that the electric thermometers all respond to temperature changes much more quickly than the mercurials.

The flexible rubber covered leads from the surface and rectal thermometers and the lead covered wires from the wall and air thermometers are carried to a ten-wire cable which perforates the calorimeter walls and is distributed on a hard rubber plate attached to the calorimeter and thence carried to the switches on the observer's table. The high tension currents from the calorimeter pass to a small hard rubber plate inside the box, thence in a separate strand cable to a slate board outside the calorimeter, and thence to the rheostat board. This cable carries leads for the telephone, electric fan and for the resistance coil used in electric checks.

ACCESSORY APPARATUS

The telephone, which has been made as light as possible, is seldom used, since the muscular work involved in telephoning is enough to affect seriously the results in rest experiments. The small electric fan placed in a corner at the foot of the calorimeter stirs the air thoroughly and allows one to get a good sample by drawing off ten liters through the large Bohr meter attached to the outgoing air pipe. The fan is run by the Edison storage batteries, giving off approximately 4.5 calories an hour, the exact amount being determined once an hour by a voltmeter and ammeter.

On the right side of the subject is a small glass shelf for the weighed urine bottles which, after each voiding, are placed on a spring balance that can be read through the window. Two small brass tubes are led through the wall of the calorimeter just below the small window. One acts as an emergency vent to prevent a positive or negative pressure at the beginning or end of an experiment when the ventilation is stopped. To the other is attached the Bowles stethoscope, which is strapped over the apex of the heart so that an observer outside can count the pulse at frequent intervals.

The inside of the calorimeter is formed by the polished tinned copper, the roof being almost hidden by the longitudinal absorber pipes wound with brass "jack chain." The calorimeter is wide enough for a man to turn comfortably from side to side, high enough at the foot to allow him to cross his legs and high enough at the head to allow him to sit upright.

THE BED

The bed in its present form is the result of much experimentation. The frame is made of varnished oak raised at the head so that the top is 12.7 cm. from the floor of the calorimeter while it is raised only 8.2 cm. at the foot. This allows for the sag of the waterproof canvas laced in the frame and keeps the subject 2 to 3 cm. from the copper floor. At the head is a back-rest with a piece of water-proof canvas, which is usually supplemented by a soft pillow. The bed is mounted on a pair of skids so that it can be pushed from the stretcher into the box. The canvas has proved to be much more comfortable than the springs and blankets formerly employed and has the advantage of absorbing very little water vapor. The varnished wood absorbs some water, the necessary clothing of the patient a great deal more, while the polished walls absorb only a minimum.

ELECTRIC AND ALCOHOL CONTROL EXPERIMENTS

The calorimeter has been tested repeatedly by dissipating known amounts of heat in resistance coils and by burning known amounts of alcohol. The apparatus and procedure used correspond almost exactly with those described by Williams and are similar to those previously used by Atwater and Benedict and by Benedict, Riche and Emmes.[8] In calculating the latent heat of the evaporation of water we have adopted the figures of Smith[9] and have given the latent heat the value of 0.584 large calories per gram of water evaporated at 23 C., the usual experimental temperature.

8. Benedict, Riche and Emmes: Control Tests of a Respiration Calorimeter, Am. Jour. Physiol., 1910, xxvi, 1.

9. Smith, A. W.: Heat of Evaporation of Water, Physical Review, 1907, xxv, 145.

TABLE 1.—ALCOHOL CHECKS *

Date and Per Cent. Alcohol by Weight	Hour	Heat				Oxygen			Carbon Dioxid			Water			R. Q. Theory, 0.667
		Alcohol Burned, Gm.	Theory, Cal.	Found, Cal.	Error, Per Cent.	Theory, Gm.	Found, Gm.	Error, Per Cent.	Theory, Gm.	Found, Gm.	Error, Per Cent.	Theory, Gm.	Found, Gm.	Error, Per Cent.	
3/8/13 92.28	1	10.14	66.25	64.52	−2.6	19.63	19.11	−2.2	17.90	17.81	−0.5	11.76	12.92	+9.8	0.662
	2	10.08	65.86	65.86	±0.0	19.41	18.08	−6.9	17.79	18.18	+2.3	11.69	11.82	+1.1	0.715
	3	9.85	64.62	64.29	−0.0	19.05	19.17	+0.6	17.46	17.44	−0.1	11.47	11.56	+0.8	0.662
	4	9.43	61.61	60.49	−1.8	18.16	17.99	−0.8	16.65	16.48	−1.0	10.94	11.10	+1.4	0.666
Average	..	......	64.52	63.79	−1.1	19.04	18.59	−2.4	17.45	17.48	+0.2	11.47	11.85	+3.4	0.676
4/30/13 91.60	1	8.42	54.60	56.06	+2.7	16.09	16.61	+3.2	14.75	14.73	−0.1	9.75	10.29	+5.5	0.644
	2	8.19	53.04	52.59	−0.8	15.65	15.43	−1.4	14.35	14.30	−0.4	9.48	10.01	+5.6	0.674
	3	8.14	52.79	51.86	−1.7	15.56	15.39	−1.1	14.26	14.37	+0.8	9.43	9.94	+5.5	0.680
	4	8.04	52.14	51.37	−1.6	15.37	15.23	−0.9	14.08	13.82	−1.8	9.31	9.55	+2.5	0.660
Average	..	......	53.14	52.97	−0.3	15.67	15.67	±0.0	14.36	14.31	−0.4	9.49	9.95	+4.8	0.665
10/14/13 90.96	1	12.24	78.83	76.50	−3.0	23.22	23.20	−0.1	21.29	21.34	+0.2	14.15	14.73	+4.1	0.669
	2	12.36	79.60	80.48	+1.1	23.45	24.82	+5.8	21.50	21.98	+2.3	14.29	14.83	+3.7	0.644
	3	11.86	76.37	73.78	−3.3	22.50	20.55	−8.6	20.63	19.98	−3.0	13.71	13.53	−1.4	0.707
Average	..	......	78.27	76.92	−1.7	23.06	22.86	−0.8	21.14	21.10	−0.2	14.05	14.36	+2.2	0.673
2/2/14 91.18	1	9.22	59.52	59.82	+0.5	17.54	17.62	+0.5	16.07	15.65	−2.7	10.43	10.85	+4.0	0.646
	2	9.29	59.97	61.29	+2.2	17.67	16.78	−5.0	16.20	15.75	−2.8	10.51	10.71	+1.9	0.682
	3	8.59	55.45	56.23	+1.5	16.34	15.98	−2.2	14.98	15.07	+0.6	9.72	10.30	+6.0	0.686
	4	9.70	62.62	64.05	+2.3	18.45	18.24	−1.2	16.91	16.82	−0.5	10.97	11.32	+3.2	0.671
Average	..	......	59.39	60.35	+1.6	17.50	17.16	−1.9	16.04	15.82	−1.3	10.41	10.80	+3.8	0.671
3/19/14 91.18	1	10.41	67.20	67.34	+0.2	19.80	19.41	−2.0	18.16	18.23	+0.4	11.77	12.02	+2.0	0.683
	2	11.02	71.14	69.43	−2.4	20.96	19.33	−7.7	19.21	18.14	−5.6	12.46	12.13	−2.6	0.683
	3	10.89	70.30	70.36	+0.1	20.71	19.53	−5.7	18.99	18.61	−2.0	12.32	12.62	+2.5	0.693
	4	10.04	64.81	66.29	+2.3	19.10	20.13	+5.4	17.50	17.75	+1.4	11.36	11.95	+5.2	0.641
Average	..	......	68.36	68.36	±0.0	20.14	19.60	−2.6	18.46	18.18	−1.5	11.98	12.18	+1.7	0.675
Total....	..	......	1216.72	1212.61	−0.33	358.56	325.60	−1.69	328.67	326.45	−0.68	215.62	222.18	+3.09	Av. 0.672

* All periods one hour long.

It has seemed advisable to publish all the electric and alcohol checks made with the calorimeter. In publishing control tests the results are much more striking if one selects only the best and leaves out those in which the agreement is not close. This method expresses only the minimum error while the things we really need to know are the average, maximum and total errors. The total error shows the accuracy of the method, the maximum error may occur in the course of any experiment, while the average error is with us always. The minimum error

TABLE 2.—ELECTRIC CHECKS

Date	Length of Period, Min.	Calories, Theory	Calories, Found	Per Cent. Error
3/4/13	60	72.25	73.19	+1.2
	60	72.25	72.19	+0.0
Average	..	72.25	72.69	+0.6
4/5/13	60	80.78	77.26	—4.4
	60	80.78	79.31	—1.8
Average	..	80.78	78.29	—3.1
10/13/13	30	41.74	42.15	+1.0
	30	41.74	41.56	—0.4
	30	41.74	41.25	—1.2
	30	41.74	41.10	—1.5
	30	41.74	41.35	—0.8
Average	..	41.74	41.49	—0.6
10/22/13	60	83.98	83.98	±0.0
	60	83.98	83.83	—0.2
	60	83.98	84.02	+0.0
	60	83.98	83.84	—0.2
Average	..	83.98	83.92	—0.1

Date	Length of Period, Min.	Calories, Theory	Calories, Found	Per Cent. Error
11/28/13	60	78.22	77.15	—1.4
	60	78.22	77.62	—0.8
	60	78.22	78.67	+0.6
Average	..	78.22	77.81	—0.5
1/26/14	60	76.92	75.86	—1.4
	60	76.92	77.41	+0.6
	60	76.92	77.88	+1.3
	60	76.92	77.24	+0.4
Average	..	76.92	77.10	+0.2
5/11/14	60A	78.71	80.03	*
	60B	78.22	75.18	....
	30C	39.07	41.35	....
Total....	150	196.00	196.56	+0.3
Total of all checks	..	1589.02	1583.42	—3.5

* A, B, C. Temperature changes of wall of calorimeter: A, +0.06 C.; B, —0.73 C.; C, —0.05 C. Test to verify hydrothermal equivalent.

is a joy to behold, but it does not occur with the regularity inferred by the prominence it is usually given. If, for instance, we should publish only the electric check of October 22 with an hourly error of 0.2 per cent., and the alcohol check of April 30, in which the total errors in the measurement of heat, oxygen and carbon dioxid are all less than ½ of 1 per cent., we should give a false impression of accuracy. This test shows that the calorimeter is capable of measuring heat, oxygen and carbon dioxid with a maximum error of 1.8 per cent. in three consecutive hours. Even better results could be obtained if greater care were taken to secure an even combustion of alcohol. On the other

hand, the errors which can occur in hourly periods and in whole experiments are shown in Table 3. The average error has been obtained by multiplying each per cent. of error by the number of times it occurs and dividing the total by the number of periods. In the whole series of experiments of three or four hours' duration the average error for heat is 0.9 per cent., for oxygen 1.6 per cent. and for carbon dioxid 0.6 per cent., while for the individual hours the error is 1.2 per cent., 3.2 per cent. and 1.6 per cent., respectively. The total error in all the

TABLE 3.—SUMMARY OF ERRORS IN ELECTRIC AND ALCOHOL CHECKS

Per Cent. Error	Average of Whole Experiment				Individual Hours			
	Cal.	O_2	CO_2	H_2O	Cal.	O_2	CO_2	H_2O
0	5	1	3	..	10	1	5	..
1	4	1	1	..	15	7	5	4
2	2	2	1	2	9	3	5	2
3	1	1	..	1	4	1	3	4
4	..	..	..	1	1	..	..	3
5	..	..	..	1	..	2	..	1
6	..	..	..	..	..	2	1	4
7	..	..	..	..	..	1	..	..
8	..	..	..	..	..	1	..	..
9	..	..	..	..	..	1	..	..
10	..	..	..	..	..	..	..	1
Total number of experiments or hours	12	5	5	5	39	19	19	19
Average error	0.9	1.6	0.6	3.2	1.2	3.2	1.6	3.7
Total error	—0.33	—1.69	—0.68	+3.09				

electric and alcohol checks is: heat, —0.32 per cent., O_2 —1.69 per cent., CO_2 —0.68 per cent. The total error in the water is + 3.09 per cent.

The electric checks show a smaller error in the measurement of calories than the alcohol, since the dissipation of heat is much more uniform. It is difficult to secure an even flow of alcohol to the burner and the larger errors in the oxygen determination are due to irregularities in the flow during the last five minutes of the period. If a slight negative pressure develops within the box toward the end of the period, alcohol is sucked into the burner causing the flame to flare up

and expand the air before the air thermometers record the rise in temperature. This causes an error in the oxygen calculation which, as the tables show, is usually corrected the next hour. With a trained human subject the production of heat and carbon dioxid and the absorption of oxygen are more regular than in the case of an alcohol check and the error presumably not so large. The cause for the negative total error in the measurement of heat, O_2 and CO_2, is not clear, but one cannot help suspecting that a slight absorption of water by the alcohol and a slight evaporation as the alcohol drops from the bottle into the buret may account for most of the error. In experiments on man there is another factor which reduces an error in the measurement of oxygen or carbon dioxid considerably. In calculating the indirect calorimetry the factor by which the oxygen or carbon dioxid is multiplied changes with the respiratory quotient and it happens that a plus error in measurement of the gas is partially offset by a minus change in the factor. This change reduces the error to an extent varying between one-fifth and three-quarters of its original size, unless the errors in both gases are in the same direction, leaving the quotient unaltered. The accuracy of the calorimeter has also been demonstrated by the close agreement of the methods of direct and indirect calorimetry. This will be taken up in detail in the paper on normal controls, but at this point it may be said that in a total measurement of 4,577 calories the two methods agreed within 0.17 per cent., and that in 26-hourly periods on the normal control most carefully studied, the agreement was within 5 per cent. in seventeen of the hours.

In spite of the fact that some of the errors published in the table are larger than those published in connection with other types of apparatus, we feel justified in believing that the Sage calorimeter is the most accurate and most reliable instrument of its size used in the study of the respiratory metabolism. The table includes all the alcohol and electric checks, good, bad and indifferent, made during the period when the machine was used for experiments. The only ones left out are those made at the beginning of the season while the apparatus was being put in order, and actual work was never begun before obtaining a check good enough to publish. To the best of our knowledge this method of publishing all the tests has never been used in connection with other types of respiration apparatus, and we have no detailed information as to their average, maximum and total errors.

It is to be regretted that we have not been able to make long electric tests to determine the hydrothermal equivalent of the calorimeter. The storage batteries are not powerful enough to furnish current for more than four hours in addition to the preliminary period of 30 to 40 minutes, and we have never felt justified in using the house current

with its variations in voltage. Numerous short tests showed that the hydrothermal equivalent was very close to 19 liters of water, and this figure gave results within 0.3 per cent. in the check of May 11 with a large temperature change in the second hour. Incidentally, the advantage of a wooden frame is shown by the rapidity with which the box responded to this temperature variation.

DETERMINATION OF WATER ELIMINATION

In all types of respiration apparatus the measurement of the water elimination has presented great difficulties. This was studied in detail by Benedict, Riche and Emmes, who found that long experimental periods were required to obtain accurate results. The interior of the Sage calorimeter is tinned and polished and there is very little woodwork and cloth, but still a considerable amount of moisture can be retained within the box. In alcohol checks with a water production of only 10 to 14 grams an hour the air becomes dryer and dryer, and this moisture is given off during the whole test, making uniformly a plus error. In experiments on normal men the water elimination is about twice this amount and the percentage of moisture changes but little from hour to hour. In patients who have a tendency to sweat, the water given off may amount to 35 to 40 grams an hour, and there is a tendency for the percentage in the air to increase steadily and finally reach the point of saturation. We should expect a plus error in the determination as the air becomes dryer, a minus error as the percentage of moisture increases, and no error while equilibrium is being maintained. After the first hour of an experiment on man it seems fair to expect an error of less than 5 per cent., except in extreme cases of sweating. More accurate results could be obtained only by removing all wood-work, stripping the man naked and increasing the ventilating current. This would involve such artificial conditions that the results would be worthless.

ADAPTABILITY OF CALORIMETER

By carefully controlling the rate of flow and the temperature of the water in the heat-absorber it is possible to adapt the calorimeter to wide variations in the heat production of the subjects. For example, on April 23, 1914, an experiment was made on a cretin with an average heat production of 26 calories an hour. The next day the subject was a patient with exophthalmic goiter, whose heat production averaged 107 calories. In one case the methods of direct and indirect calorimetry agreed within 0.2 per cent., and in the other within 0.7 per cent. It has also been possible to adapt the calorimeter rapidly to changes in the heat production from hour to hour by changing the temperature of the

ingoing water and in extreme cases by changing the rate of flow at the beginning of a period.

It has been possible in a long series of experiments for two men to take all the readings and make all the calculations in hourly periods. Three men can handle the apparatus with ease during the trying experiments, and most of the alcohol checks, which are much more difficult, have been made with only three in the room. As a rule, the staff arrives shortly before nine o'clock in the morning, makes a three-hour experiment, gets everything in readiness for the next day and leaves the calorimeter room about three or four o'clock in the afternoon. It has been possible, on occasions, to make six experiments in a week. The calorimeter has been very seldom out of commission. Between October 13, 1913, and May 18, 1914, it was possible to make 113 experiments on man and eight alcohol and electric checks.

SUMMARY AND CONCLUSIONS

The original Atwater-Rosa respiration calorimeter with the improvements added by Benedict, Williams and others has been adapted for clinical study in Bellevue Hospital. The form of the apparatus makes it perfectly comfortable for patients. The accuracy is such that in observations lasting three or four hours the heat production, carbon dioxid elimination and oxygen consumption as determined by alcohol and electric tests can be measured with an average error of 0.9 per cent., 0.6 per cent. and 1.6 per cent., respectively. In periods one hour long the average error for heat measurement was 1.2 per cent., for carbon dioxid 1.6 per cent. and for oxygen 3.2 per cent.

The calorimeter never needs more than three men for its operation, and two men have repeatedly made all the readings and all the calculations in hourly periods.

CLINICAL CALORIMETRY

THIRD PAPER

THE ORGANIZATION OF A SMALL METABOLISM WARD *

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All investigators who have attempted to carry on metabolism experiments in hospitals have experienced more or less difficulty in the administration of the diets and the collection of the excreta. The necessity for a special metabolism ward became evident as soon as it was decided to build a respiration calorimeter in Bellevue Hospital. Through the generosity of the trustees of the hospital and the attending staff of the Second Medical Division a small ward holding four or five beds was placed in charge of the medical director of the Russell Sage Institute of Pathology,[1] who was also one of the junior members of the attending staff of the hospital. He is directly responsible to the attending physician for the welfare of the patients, and there has always been a spirit of active cooperation between the small metabolism ward and the large medical wards of the service.

The calorimeter room described in the preceding paper[2] is located on the same floor as the male medical wards of the Second Division in the new Medical Pavilion. The side hall, used as an entrance to the calorimeter room, has been partitioned off to make a small diet kitchen. Next to this is a well lighted ward of four beds used almost exclusively for patients whose metabolism is the subject of active investigation.

The patients are cared for by three graduate nurses, trained in metabolism work and paid by the Institute. The success of the ward is in large measure due to the faithful and intelligent work of the head nurse, Miss Estelle Magill, and her two assistants. They have used the same care in the preparation of food and the collection of excreta that is used in the laboratory and the effort has constantly been made to keep the error within 1 per cent. In order to maintain a high degree of accuracy and at the same time a high standard of nursing it is necessary for the three nurses to devote their whole time to the ward of only four patients. Orderlies, the greatest source of error in metab-

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* From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital, New York.

1. Dr. Eugene F. DuBois.
2. Riche and Soderstrom: See p. 13.

olism work, are excluded from the ward and patients are never allowed in the hospital dining room or kitchen, and only the most trusted are permitted to leave the room at all. These precautions are necessary in order to afford the certainty that the twenty-four-hour specimens of urine are complete and that the patients have not smuggled in outside food. Patients are not allowed out of sight of the nurse in charge for more than a couple of minutes at a time.

The food supplied to patients in the metabolism ward is all prepared by the special nurses, who have become so skilled in the preparation of the various dishes that they can even make one-sided diets attractive. In fact, the patients enjoy the cooking so much that they are sent to their homes or to the general hospital ward with difficulty This is a matter of importance when one desires to keep interesting cases under observation. The foods are prepared as often as possible from raw materials whose composition is determined from time to time. Milk and cream have been of fairly constant composition, as the analyses over a period of several years have shown.

By applying some of the principles of business efficiency, the work has been made a great deal easier. The dry cereals, eggs, bacon, etc., are weighed in white enamel dishes and bowls of known weight marked with serial numbers. Milk and cream are measured in measuring cylinders and added to these dishes in which the food is baked, fried or boiled. The dishes with the cooked food are then taken directly to the patient and if by any chance he should leave some of the food it is an easy matter to weigh it back. Egg whites and yolks are weighed separately. Sugars, salt, cocoa, butter, etc., are put up in packages of known weight by the night nurse to save time during the day.

When a patient first enters the ward the nurses spend a couple days in investigating his dietetic limitations and his dislikes, a matter of great importance. A diet such as the following, for example, is then ordered: 3,000 calories, 15 grams nitrogen, ½ non-protein calories in fat, ½ in carbohydrate. The nurses then work out a diet which will fulfil the specifications and at the same time be agreeable to the patient. Often by careful work it is possible to educate a patient to a diet that he could not otherwise tolerate. We cannot too strongly emphasize the need of individualization aided by good cooking in experimental metabolism work.

The method of collecting twenty-four-hour specimens is, we believe, a new one, and since it has proved to be very satisfactory, should be given in detail. A large number of 20-ounce, round, wide-mouthed bottles with cork stoppers are kept in the ward. These have been etched on the side so that one can write on them with a pencil. At 5 a. m., the time at which the twenty-four-hour period ends, each

COMPOSITION OF FOODS USED IN METABOLISM WARD

Food	Protein	Fat	Carbo-hydrate	Calories per Gram	100 Calory Portion
Beef, chopped	22.1–48.6	2.4–12.8	0	1.3– 2.0	50– 79
Beef broth	2.1	0.2	0	0.1	1000
Bread, white	9.8	0.3	53.5	2.6	38
Chicken, minced	18.5	7.2	0	1.5– 1.5	69
Cabbage, thrice boiled *	....	....	0.24		
Cauliflower, thrice boiled *	1.75	....	0.12		
Cocoa, powdered	23.1–23.2	19.4–25.2	48.3–54.0	4.8– 5.3	19– 21
Cheese, cottage	14.9–19.2	0.2– 1.9	0	0.6– 0.9	118–164
Crackers, soda	8.3	9.3	73.2	4.3	24
Crackers, sugar	6.2	10.7	80.1	4.5	22
Cream	2.1– 2.9	17.1–19.8	4.0–5.2	1.9–2.1	48– 53
Cream	2.1–2.9	17.1–19.8	4.0–5.2	1.9–2.1	48–53
Custard	5.4	3.5	21.6	1.4	70
Custard, hospital diabetic	5.7	5.7	7.3	1.1	94
Farina, dry	18.9	0.9	68.2	3.7	27
Flour, hospital diabetic	23.2	1.3	68.2	3.9	26
Ice cream, vanilla	3.4– 4.8	1.7– 6.9	12.2–23.4	1.0– 1.6	61– 99
Ice cream, chocolate	3.7	5.5	12.3	1.2	85
Jelly, lemon	2.1	0.2	17.1	0.9	111
Junket	2.1	2.1	16.6	1.0	104
Macaroni, dry	13.7	1.2	77.5	3.9	26
Mammala	26.8	9.6	....	4.2	24
Mammala (separated milk)	31.7	5.4	....	4.0	26
Mammala (full cream)	10.2	28.2	....	5.5	18
Milk, hospital	3.09– 3.1	3.3– 4.67	4.10– 4.7	0.6	166
Oatmeal, dry	15.1	5.6	71.2	4.1	24
Potatoes, mashed	2.2	0.2	18.0	0.9	118
Pudding, rice	4.1	3.0	24.8	1.5	68
Pudding, tapioca	5.7	2.3	14.8	1.1	94
Rice, dry	7.0	0.5	81.9	3.8	27
Rice, cooked	1.4	0.3	13.1	0.6	159
Tapioca	....	....	91.1	3.7	27
Special Articles—					
Cane sugar	Sucrose 100 per cent.			3.96	25.2
Corn sirup—glucose	Glucose, 41.3 per cent.; dextrin, 33.9 per cent.; sucrose, 2.7 per cent.			3.07	32.6
Corn sirup—glucose	Glucose, 42.4 per cent.; dextrin, 44.6 per cent.; sucrose, 0.				
Gelatin					
Lactose	Lactose, 98.4 per cent.			37.0	27.0
Olive oil	....			9.52	10.5
Sherry	Alcohol by volume, 19.45 per cent.; Carbohydrate, 1.96 per cent.			1.46	68.5c.c.
Vinegar	Acetic acid, 4.07 per cent.				
Whisky	Alcohol by volume, 41.76 per cent.			2.96	33.8c.c.

* Cooked in three changes of water.

patient is given a bottle and made to empty his bladder. The bottle is then marked with his name, the date, the hour and minute. The volume is estimated for clinical purposes by comparison with a calibrated bottle of the same capacity. The data are then recorded on a special slip of paper to go to the laboratory and also on the diet chart. A little toluene is added to the urine bottle, which is corked and stored in the ice-box along with the previous voidings of that twenty-four-hour period, each voiding being in a separate bottle. At about 9 o'clock in the morning the laboratory man checks up the bottles with the records on the laboratory slip, and with the nurse's notes takes all the bottles to the laboratory, measures the volume accurately, makes up to volume and analyzes a sample.

The only disadvantage of this system is the labor of carrying a number of half-filled bottles, although this is not great if suitable carriers are used. The advantages are as follows: 1. There is no chance of a specimen of urine having been poured into another patient's bottle thus spoiling two twenty-four-hour specimens. 2. If a single voiding is lost the urine for the remainder of the day can be accurately analyzed. 3. The urine can be fractionated and the nitrogen elimination determined in hourly periods, as is frequently done in calorimeter experiments. 4. The bottles make excellent urinals, are less apt to spill than the ordinary ward urinal and are not unsightly even when filled with urine. 5. Since the urines are made up to volume in the laboratory, it is possible to rinse out each bottle with distilled water and collect every drop of urine. 6. The bottles are washed, dried, and, if necessary, sterilized in the laboratory, so that there is no danger of a patient voiding into a urinal containing decomposing urine. 7. The bottles are cheap and can be kept on hand in large numbers, so that the patients need never wait for the urinal. 8. While we have never had occasion to use them in a general ward, there is no reason why they should not be used instead of the common type of expensive and unsightly urinal. In collecting single specimens for the usual routine analysis the nurse could put a bottle by each bed in the morning and send the desired specimens directly to the ward laboratory without transferring to a special jar. It is surprising how long urines will remain clear if voided into and kept in a clean bottle.

The collection of feces is somewhat more difficult. Patients who can get out of bed defecate into a weighed bucket in the commode. This bucket is then weighed again. A little formalin is added and the whole sent to the laboratory where the specimen is thoroughly mixed and one-tenth removed to be dried and added to the other aliquot portions of that period and analyzed. Bed-ridden patients use a weighed bed pan from which the feces are transferred to a covered bucket for

transportation. Most of the patients with acute diseases are given every morning an enema of hypertonic salt solution. Oil and soap enemas of course interfere with the accuracy of the fat analyses; glycerin enemas make it impossible to dry the feces. To divide the periods, powdered carmin (0.3 gm., 5 grains) is given with the first meal of the period and with the first meal after the period is ended. Experience has shown that it is much easier to determine the exact point of appearance of the carmin in the feces than to find the point of disappearance. When patients are being given enemas it is easier to discover traces of carmin than traces of charcoal. Periods are made as long as possible to minimize the errors of division.

A special diet sheet has been provided by the hospital on which the nurses record the weights of raw material given to the patient and make the calculations from the table of known composition of the food. On this sheet is a summary column giving carbohydrate, fat and protein grams and calories, total calories, nitrogen of the food, of the urine, of the total excreta and the nitrogen balance; weight of the patient and food calories per kilogram. In another place are columns for recording the time and amount of each voiding and each defecation.

Patients are weighed at 9.00 a. m. every day or every other day on a "silk scale" accurate to 10 grams. Bed patients are weighed on a platform resting on these scales in the manner described by Coleman.[3] The nurse slides the patient on the smooth platform which is just at the level of the bed, weighs him and then makes up the bed while he is still on the balance. The whole procedure has been found to be a convenience for the nurse rather than a time-consuming task.

Nitrogen determinations are made by the Kjeldahl method, ammonia, uric acid, creatin, creatinin, and indican by Folin's[4] methods, urea and glucose by the methods of Stanley R. Benedict.[5]

The calorific value of the foods has been determined by means of the Riche[6] bomb calorimeter. Food fat analyses have been made in a Soxhlet apparatus. Carbohydrates were determined by a difference using in the later work a new procedure described by Gephart.[7] The

3. Coleman: Diet in Typhoid Fever: Journal Am. Med. Assn., 1909, liii, 1145.

4. Folin: Approximately Complete Analysis of Thirty Normal Urines, Am. Jour. Physiol., 1905, xiii, 45.

5. Benedict: The Detection and Estimation of Glucose in Urine, Jour. Am. Med. Assn., 1911, lvii, 1193. The Estimation of Urea in Urine, Jour. Biol. Chem., 1910, viii, 405.

6. Riche: An Improved Type of Calorimeter for use with any Calorimetric Bomb, Jour. Am. Chem. Soc., 1913, xxxv, 1747.

7. Gephart, Frank C., and Csonka: In the Estimation of Fat in Feces, Jour. Biol. Chem., 1914, xix, 521.

dried feces were powdered and the fat determined at first by the Kumagawa-Suto method and later by the new saponification procedure described by Gephart.[7] In calculating food values, Rubner's factors were used, namely: for fat 9.3 calories; for carbohydrate and protein, 4.1 calories per gram.

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8. Kumagawa and Suto: Ein neues Verfahren zur quantitativen Bestimmungen des Fettes und der unverseifbaren Substanzen in tierschen Material nebst der Kritik einiger gebrauschlischen Material, Biochem, Ztschr., 1908, viii, 212.

CLINICAL CALORIMETRY

FOURTH PAPER

THE DETERMINATION OF THE BASAL METABOLISM OF NORMAL MEN AND THE EFFECT OF FOOD *

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The importance of the normal control has been emphasized so strongly by the serologists and the management of the control has been developed by them to such an art that it has seemed advisable to apply some of their methods of critique to the study of the respiratory metabolism. Serologists insist that a man shall make his own controls with the same apparatus and exactly the same technic as in the experiments and they also insist that the controls shall be numerous enough to show individual variations in their true proportions. These precautions and many others have been made necessary by the fact that the normal control is usually the point of attack in serological controversies. Likewise in the study of metabolism the normal control is coming to be recognized as the weakest part of the experiment. The chemical methods of blanks and duplicates will not suffice; the living organism is the uncertain factor. The literature is notoriously filled with false theories, of which by far the greater part would never have been promulgated if sufficient attention had been given to normal controls.

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† With the technical assistance of G. F. Soderstrom and R. H. Harries.

The three papers immediately preceding have described the Sage respiration calorimeter in Bellevue Hospital and its adjoining metabolism ward. Before presenting any of the work in pathological conditions it has seemed best to study in detail the results obtained on the normal controls. It was the original intention to use a large number of normal subjects and determine the individual variations in metabolism, but this laborious piece of work was gladly abandoned when it was learned that Benedict and his collaborators were engaged in the task. In pathological conditions the work has been confined as much as possible to men between the ages of 20 and 50 who do not depart very markedly from the normal relationship between height and weight. Consequently the normal controls have been selected to comply with these requirements.

BASAL METABOLISM

As a basis of comparisons between all normal individuals and groups of patients the heat production in the morning from fourteen to eighteen hours after the last meal with the individual at complete rest, was selected. This has been termed the *"nüchtern"* metabolism by the Germans, the "post-absorptive" by Benedict and Cathcart,[1] but the simplest and most satisfactory term is "basal metabolism," a translation of the German *Grundumsatz,* as used by Lusk and his coworkers[2] in the series of papers published under the heading of Animal Calorimetry.

The literature of the respiratory metabolism of healthy men has been admirably reviewed by Benedict and Carpenter[3] in 1910 and Loewy[4] in 1911. In the former monograph the results of a large number of experiments with the respiration calorimeter of Wesleyan University are gathered in numerous tables. During the so-called rest experiments, however, the subjects were allowed to move about the room and indulge in minor muscular activities, something which had

1. Benedict and Cathcart: Muscular Work, Carnegie Institution of Washington, 1913, Pub. 187.

2. Lusk: Calorimetric Observations, Med. Rec., New York, 1912, lxxxii, 925; Williams, Riche and Lusk: Animal Calorimetry, Second Paper. Metabolism of the Dog Following the Ingestion of Meat in Large Quantity, Jour. Biol. Chem., 1912, xii, 349; Lusk: Third Paper, Metabolism After the Ingestion of Dextrose and Fat, Including the Behavior of Water, Urea and Sodium Chlorid Solutions, Ibid., 1912, xiii, 27; Lusk: Fifth Paper, The Influence of the Ingestion of Amino-Acids upon Metabolism, Ibid., 1912, xiii, 155; Lusk: Sixth Paper, The Influence of Mixtures of Foodstuffs Upon Metabolism, Ibid., 1912, xiii, 185.

3. Benedict and Carpenter: The Metabolism and Energy Transformations of Healthy Man During Rest, Carnegie Institution of Washington, 1910, Pub. 126.

4. Loewy: Oppenheimer's Handbuch der Biochemie der Menschen und der Thiere, Jena, 1908, iv,[1] 172.

been permitted in practically all the large respiration chambers. Benedict and Carpenter measured the increased heat production caused by certain simple movements which their subjects had performed during the experiments. The act of rising from a chair, taking one or two steps, opening the food aperture, removing the food, closing the window and returning to the chair required only 19 to 29 seconds, but involved the expenditure of 1.22 calories. Considering the short time involved in the operation, the heat production was increased from 200 to 300 per cent. They also found the metabolism 15 per cent higher when the subject was standing than when he was sitting, and from 8 to 10 per cent. higher when lying awake than when sleeping. The sleeping periods were between 1 a. m. and 7 a. m., and the waking periods followed immediately in the three experiments which were really satisfactory. During the waking periods there was an increase in the oxygen consumption amounting to 1.7, 0.9 and 11.5 per cent., while the heat production was increased 5.8, 15.2 and 13.1 per cent. Some of this increase may be accounted for by difference in the time of day, some by small muscular movements. Johansson[5] found that with complete muscular relaxation the carbon dioxid production was the same as during sleep. The two individuals (H. C. K. and H. R. D.) studied by Benedict and Carpenter produced during sleep 35.2 and 36.2 calories per square meter of body surface, whereas only three of the twelve normal men, whose metabolism is recorded in Table 3, produced more than 35.1 calories per square meter per hour. It is obvious that if the metabolism of H. C. K. and H. R. D. were increased 5.8 per cent., 15.2 per cent. and 13.1 per cent., this increase would carry them just so much farther into the zone where it is necessary to assume muscular activity to account for the abnormally high metabolism.

In anticipation it may be well to mention that the average basal heat production of the individuals we are reporting is 34.7 calories per square meter per hour, the subjects lying awake, at perfect rest during the morning hours. The average heat production of the nineteen subjects of Benedict and Carpenter while asleep between the hours of 1 a. m. and 7 a. m. was 35.3 calories and of fifty-five individuals while awake and moving from time to time in the calorimeter was 49.2 calories per square meter per hour. The fact that their sleeping subjects showed a metabolism 3 per cent. higher than our subjects awake may substantiate the conclusions of Johansson. Benedict and Carpenter pointed out at the conclusion of their monograph (p. 246) the fact that the figure 49.2 calories per square meter per hour, equaling

5. Johansson: Ueber die Tageschwankungen des Stoffwechsels und der Körpertemperatur in nüchternem Zustande und vollsändige Muskelruhe, Skand. Arch. f. Physiol., 1898, viii, 85.

36.5 calories per kilogram per day, represented not the condition of true rest, but rather that of a person confined for the day to a small room but allowed to dress and undress, sit in a chair, feed himself, etc.

Since the appearance of this monograph Benedict and his coworkers, and also other investigators, have insisted more and more strongly on the necessity of absolute quiet in rest experiments and as a check on muscular activity a graphic record of all movements. This eliminates for our purposes practically all the work done in large respiration chambers before 1910 and leaves us only the work done by means of the small types of apparatus, and especially the Zuntz-Geppert apparatus, by Magnus-Levy and Falk,[6] and by Loewy. The results of the determinations on nineteen normal individuals have been collected in a table by Loewy[7] which is reprinted by Benedict and Joslin.[8] Coleman and DuBois,[9] in gathering normal controls to compare with their typhoid patients, grouped these cases of Loewy with twenty-seven normal controls taken from the work of Benedict and Joslin, and with two of their own cases. The average heat production of the total forty-eight normal men was 33.7 calories per square meter of body surface per hour. Very recently Benedict, Emmes, Roth and Smith[10] published a brief report of their important work on the basal metabolism of a total of eighty-nine men and sixty-eight women. The early appearance of these determinations has been of great service to us, and we wish to express our appreciation to these investigators for the publication of the most essential part of their data.* All their determinations were made on healthy subjects in the morning at least twelve hours after the last meal, with the subject at complete rest. Some of the experiments were made in the bed calorimeter of the Nutrition Laboratory of Boston, but most of them were short experiments made with the small Benedict "universal respiration apparatus." The fact that this small machine gives results almost identical with the calorimeter was amply proved by Benedict[8] and his coworkers and confirmed by the limited amount of work done with both types of apparatus by

6. Magnus-Levy and Falk: Der Lungengaswechsel des Menschen in verschiedenen Alterstufen, Arch. f. Anat. u. Physiol., 1899, Supp. 314.

7. Loewy: Oppenheimer's Hand. der Biochemie der Menschen und der Thiere, Jena, 1908, iv,[1] 179.

8. Benedict and Joslin: Metabolism in Diabetes Mellitus, Carnegie Institution of Washington, 1910, Pub. 136; A Study of Metabolism in Severe Diabetes, ibid., 1912, No. 176. Ueber der Stoff- und Energieumsatz bei Diabetes, Deutsch. Arch. f. klin. Med., 1913, cxi, 333.

9. Coleman and DuBois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, The Archives Int. Med., 1914, xiv, 168.

10. Benedict, Emmes, Roth and Smith: The Basal, Gaseous Metabolism of Normal Men and Women, Jour. Biol. Chem., 1914, xviii, 139.

* A more complete discussion of the work is appearing in the Jour. Biol. Chem., March, 1915.

Coleman and Du Bois.[9] The average heat production of the eighty-nine men was 34.7 calories per square meter per hour, and of the sixty-eight women, 32.2 calories. The lower heat production of women is in accord with the previous findings of Sonden and Tigerstedt.[11]

The work of Magnus-Levy and Falk[6] showing the diminution of metabolism in old age and the increase in youth is also confirmed. The two men over 50 years of age produced only 28.9 calories per square meter. The eight youths between 17 and 20 averaged 37.1 calories, nine who were 20 years old, 36.6 calories, seven who were 21 years old, 36.1 calories.

SPECIFIC DYNAMIC ACTION OF FOODS

The subject of the specific dynamic action of foods in increasing metabolism is fully discussed by Lusk[12] in his text-book and in a series of papers on animal calorimetry.[2, 13]

From his work on dogs, Lusk has concluded that the specific dynamic action of protein is due to the stimulation of the metabolism of the cells by certain of the amino-acids while the action of fat and carbohydrates is due to the mass action of these metabolites in the circulation. He has found marked differences in the action of the various amino-acids and the various carbohydrates. The study of the specific dynamic action of foods on man is not nearly as far advanced as in the case of the dog. Magnus-Levy[14] in connection with his work on dogs found that after giving a man 50 to 60 grams of carbohydrate the metabolism was increased in the first hour from 2 to 12 per cent., in the second hour 0 to 7 per cent. After 140 to 160 grams of starch in bread the increase in the first hour averaged 22 per cent., the second hour 14 per cent., the third hour 16 per cent. After 210 grams of bacon and butter the metabolism was increased 5 to 10 per cent. for seven to eight hours, while after 210 to 250 grams of beef the oxygen consumption rose from 3 to 12 per cent. the first hour and then 15 to 34 per cent. in the next six hours. Gigon[15] obtained similar results using a Jacquet apparatus. In the period of four to five hours following the ingestion of 100 grams of dextrose there was an increase of 9.5 per cent. in the oxygen consumption. After 50 grams of casein the oxygen was increased 5.5 per cent. and after 100 grams 16.8 per cent.

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11. Sonden and Tigerstedt: Untersuchungen über die Respiration und den Gesammtestoffwechsel des Menschen, Skand. Arch. f. Physiol., 1895, vi, 99.
12. Lusk: The Science of Nutrition, Philadelphia, 1909, second edition; Stoffwechsel und Ernährung; Deutsche Uebersetzung von L. Hess, 1910.
13. Lusk: The Cause of the Specific Dynamic Action of Protein, The Archives Int. Med., 1913, xxi, 485.
14. Magnus-Levy: Ueber die Grosse des respiratorische Gaswechsels unter dem Einfluss der Nährungsaufnahme, Arch. f. d. ges. Physiol. (Pflüger's), 1894, lv, 1.
15. Gigon: Ueber den Einfluss der Nährungsaufnahme auf den Gaswechsel und Energieumsatz, Arch. f. d. ges. Physiol. (Pflüger's), 1911, cxl, 509.

EXPERIMENTAL PROCEDURE

The normal controls who were kept in the metabolism ward were given a maintenance ration, the last meal of the day being about 5 p. m. At 5 a. m. they were awakened, given an enema, and instead of breakfast, a cup of coffee without cream or sugar. At about half past nine the calorimeter bed was wheeled to the ward on the weighing platform, which is provided with large casters, and the subject lifted from his bed, weighed, rolled back to the calorimeter room and slid into the calorimeter, bed and all. He was dressed in a night shirt, thick ward pajamas and thick socks, and, as a rule, the legs were covered with a sheet, although some subjects needed a thin blanket and others required no covering. A soft pillow was placed under the head and sometimes one under the knees. Every effort was made to ensure absolute comfort, a matter of great importance in work on the respiratory metabolism.

Those normal controls who lived at home took their evening meal at 6 or 7 o'clock, rose at 6 or 7 a. m., drank a cup of black coffee, took the street car, walked about ¼ mile and arrived at the hospital at 9 o'clock. They then undressed, weighed themselves, dressed in warm pajamas and entered the calorimeter.

As soon as the subject was in the calorimeter the rectal thermometer was inserted about 12 cm. in the rectum, giving slight discomfort for a few minutes, but later remaining in position without the man's being conscious of its presence. The surface thermometers were next fastened tightly to the thorax, axillae or abdomen by means of adhesive plaster and the whole covered with a pad of absorbent cotton about 20 cm. in diameter and 3 or 4 cm. thick, this being held in place by strips of adhesive. The Bowles stethoscope was next strapped over the apex of the heart and the whole covered with night shirt and pajamas. When this was finished the bed was shoved all the way into the box, the ventilation started, and at about a quarter past 10 the glass plates were sealed in the end of the calorimeter and the heavy front put in position, making it possible to start the preliminary period shortly after half past ten.

The actual preparation of the calorimeter had begun long before this. On the previous afternoon all sulphuric bottles, soda-lime containers, etc., had been filled and the oxygen tank weighed so that any leakage over night might be detected. The temperature of the calorimeter room had been watched every hour by the night nurse and maintained within 1 degree of the standard experimental temperature of 23 C. At nine in the morning the water circulation through the various cooling coils and the absorber had been started and a lighted 32 candle power electric lamp placed in the box until the subject was ready. If

these precautions had been carefully followed and if the observer had watched the temperature of the various parts of the apparatus, it was possible to bring the box into perfect equilibrium and control fifteen to twenty minutes after the start of the preliminary period. As we shall see later, there is reason to believe that during the first hour after the box is sealed the wooden frame of the bed may absorb a little heat owing to its proximity to the subject's body.

As a rule the preliminary period lasts thirty to forty minutes and the experiment begins shortly after 11 o'clock. Eight minutes before the start a sign is hung in the window telling the subject to remain absolutely quiet and the first residual sample of ten liters of air is drawn through U tubes by means of the Bohr meter. At four or five minutes before the start the second residual is begun and a tracing of the spirometer curve made in the manner first used by Benedict and Carpenter. At "time" the various cocks and switches are turned

TABLE 1.—The Statistics of the Normal Controls

Subject	Weight, Kg.	Height, Cm.	Chest Circumference, Cm.	Age, Yrs.
G. L.	78.4	175.5	90.5	47
E. F. D. B.	73.6 75.5	178.8	91.5	31-32
F. C. G.	56.5	173.9	80.2	29
R. H. H.	62.0	177.2	85.3	21
L. C. M.	59.5	170.6	86.6	22
Louis M.	51.7	....	....	22
John L.	70.9	....	....	44

as described in the previous article. One or two minutes after "time" the subject is allowed to shift his position, and, if necessary, void into a tared urine bottle which he then places on a small spring balance so that the exact weight of urine passed can be read through the calorimeter window. During the remainder of the hour he lies as quiet as possible trying not to turn from back to side and vice versa more than once an hour. The work-adder on the spirometer records each movement and the electrical control of the calorimeter is so delicate that the observer in charge of the thermometers can detect such slight activity as turning the head to look out of the window by the rise in the temperature of the air and wall. At the close of the first and subsequent hours the procedure is the same as at the start, except that only one sample of residual air is analyzed.

The statistics of the normal controls are as shown in the accompanying table (Table 1).

DESCRIPTION OF SUBJECTS AND DETAILS OF EXPERIMENTS

G. L., physiologist, large frame, slightly adipose. Has taken but little exercise during the last few years. Health good, no recent illnesses. Physical examination negative.

Experiment 1.—March 11, 1913. Although this was the first experiment on man made with the Sage calorimeter, the accuracy of the machine had been thoroughly tested by means of the alcohol checks described in Paper 2. The temperature of the air in the calorimeter was 24.5 C. in this experiment instead of the temperature of 23 C. used later. In addition to a suit of pajamas, the subject wore a heavy sweater. The basal metabolism was determined in the first two hours and at the beginning of the third hour he drank a solution of 115 grams commercial glucose (dextrose 42.37 per cent., dextrin 44.57 per cent., water 13.50 per cent.) in 500 c.c. water and 10 c.c. lemon juice. The commercial glucose was equivalent in calories to 100 grams dextrose. The subject, who had felt somewhat too warm during the first two hours, perspired profusely after the glucose. He remained very quiet during the five hours.

E. F. D. B., physician, large frame, moderate adipose. Up to the age of 22 in good athletic condition; since then has exercised in steadily decreasing amounts. During the winter of 1913 took violent exercise for about half an hour twice a week; in 1914 scarcely exercised at all. General health good; no recent illnesses. Heart, lungs, etc., normal.

Experiment 2.—March 13, 1913. The basal metabolism was determined in the first two hours, and at the beginning of the third hour he drank 115 grams commercial glucose in the same solution as in the experiment on G. L. The temperature of the calorimeter was 22 C. and his clothing consisted of thin undershirt and pajamas. He did not perspire but blew his nose several times each hour, spent a good deal of the time looking out of the window and was distinctly more restless than in the subsequent observations.

Experiment 25.—May 17, 1913. Basal determination only. Was very quiet during all three hours and dozed from 11:30 to 11:50.

Experiment 27.—May 22, 1913. At 8:55 a. m., before entering the calorimeter, drank 230 gm. commercial glucose (equivalent to 200 gm. dextrose) in 500 c.c. water and 15 c.c. lemon juice. Six minutes were required to drink the mixture. Dozed at times during the experiment.

Experiment 115.—March 30, 1914. Basal metabolism only. This experiment was conducted by only two observers, Mr. Soderstrom and Mr. Harries, and the periods were made one and one-half hours long to give them more time for weighings, etc. In the subsequent experiments on this subject these two observers alone were able to make all measurements and keep up with the calculations in hourly periods, a record of which they may well be proud, especially since the agreement between the direct and indirect calorimetry was unusually good.

Experiment 116.—April 1, 1914. Just before entering the calorimeter between 9:45 and 10:07 a. m., the subject ate the following meal containing 10.5 gm. nitrogen: fat-free milk, 600; pot cheese (cottage cheese or *Schmierkäse*), 150; egg-white, 120; egg-yolk, 20. During this experiment the work-adder was out of order and recorded part of the excursions of the spirometer due to the admission of oxygen to the box. The subject was very quiet, much more quiet than the work-adder record would indicate.

Experiment 138.—May 8, 1914. Between 10:05 and 10:07 a. m., drank a solution of 200 gm. C. P. Dextrose (Merck) in 400 c.c. water and 35 c.c. lemon juice. No glycosuria resulted in this or any other of the experiments on normal controls.

Experiment 141.—May 15, 1914. An attempt was made to raise the respiratory quotient as high as possible by filling the glycogen stores of the body

before giving the dextrose. At 11:30 the night before the experiment and again at 6:15 in the morning the subject ate the following carbohydate meal: shredded wheat, 55 gm.; milk, 100 c.c.; cane sugar, 10 gm.; in the morning taking an additional 10 gm. cane sugar in coffee. Between 9:50 and 9:53 he drank a solution of 200 gm. C. P. Dextrose in 400 c.c. water and 35 c.c. lemon juice.

F. C. G., chemist, thin. At age of 16 had an attack of malaria lasting two weeks. Has not been sick in bed since then and has never weighed over 64 kg. (140 pounds). Has never taken systematic exercise, except baseball from 1900 to 1906. Appetite fair, sleeps well. Physical examination: complexion pale and somewhat sallow; hemoglobin normal; state of nutrition rather poor; heart, lungs and abdomen normal. Experiment 142, May 18, 1914. Basal determination.

Experiment 3.—March 17, 1913. The basal metabolism was determined between 9:02 and 12:02, the subject going into a profound sleep in the second and third hours. The calorimeter was then opened and the subject ate the *Haferschleim* mixture of Schmidt's test diet. This contained 40 gm. dry oatmeal, 10 butter, 200 milk and one egg, or approximately, protein, 13.1, fat, 10.2, carbohydrate, 35.5 gm. At the end of the observation it was apparent that the respiratory quotients were abnormally low and that the apparent oxygen consumption was much higher than was consistent with the direct calorimetry. The cause for this was found in a leak in the oxygen cylinder, making it necessary to omit the oxygen figures from the data and base the calculations on the direct calorimetry alone.

Experiment 17.—April 22, 1914. Basal determination. The subject remained very quiet, but took care not to go to sleep. Unfortunately the oxygen cylinder leaked again and the calculation of the indirect calorimetry was not accurate.

R. H. H., chemist, tall and spare with long and rather thin bones, very little adipose. At the age of 12 had pneumonia, since then always well. Up to four years ago played semiprofessional baseball or basketball almost every day. Since 1910 his exercise has been limited to four to ten miles of walking a day and in summer a swim of about two miles a day. Physical condition good, heart, lungs and abdomen normal.

Experiment 4.—March 13, 1913. Basal determination. During the experiment this subject tried to void at the beginning of each hour but was unable to do so and was slightly more nervous and more active than the other subjects. He could not void before his first meal after the experiment and it has therefore been necessary to omit the figures for the urinary nitrogen and base the calculations on the tables of Magnus-Levy,[16] assuming that 15 per cent. of the calories were derived from protein.

Louis M., barber, small frame, short and thin, muscles fairly firm. This subject was in the hospital from September 7 to October 30, 1912, with a moderately severe attack of typhoid fever, and served as a subject of numerous observations by means of the Benedict universal respiration apparatus (Coleman and DuBois[9]). He was born in Germany and came to New Orleans in 1911. There he suffered from a severe attack of malaria but has had no recurrences. His family history shows that one sister is insane.

After his attack of typhoid he left the hospital in excellent condition and he has been perfectly well for the last four months, although at first he was somewhat weak and easily tired. Physical examination shows heart, lungs, abdomen, etc., to be normal.

Experiment 7.—March 26, 1913. Basal metabolism. Subject remained in the metabolism ward four days. On the evening previous to this experiment

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16. Magnus-Levy: Von Noorden's Handbuch der Pathologie des Stoffwechsels, Ed. 2, 1906.

at 5 p. m., ate a dinner containing protein, 35.1 gm., fat, 37.1, carbohydrate, 105.6. During the experiment he lay very quiet, dozing most of the time.

Experiment 8.—March 28, 1913. March 27 his food contained protein, 80.6; fat, 168.9; carbohydrate, 268.7 gm.; the last meal of the day at 6 p. m. containing protein, 28.9; fat, 61.7; carbohydrate, 82.3 gm. Just before entering the box, between 8:25 and 9:25 a. m., he ate 725 gm. chopped beef, fried in butter, the whole containing 23.93 gm. nitrogen and 100 gm. fat. During the experiment he slept from 12:26 to 1:18 p. m. and from 3:22 to 3:30. There was a small leak from the absorber pipe into the calorimeter, making the apparent water elimination about 1 gram an hour too high.

John L., dentist, medium frame, medium height, well nourished, muscles flabby. This subject, who was born in Sweden, served as a normal control in the metabolism experiments of Dr. R. A. Cooke,[17] who investigated the functional powers of the kidneys. Careful tests showed in this subject a slight delay in the excretion of sodium chlorid, but there were no other signs of kidney disease. He gave a history of moderate indulgence in alcohol. In 1904 he was jaundiced; a few months prior to the experiment he suffered from an infected hand after a dog bite. For the last five years he has been nervous. He was admitted to the hospital Jan. 15, 1914, suffering from a few small boils and a pedicular eruption. His ailments were so slight that he was induced to remain in the hospital as a normal control and, being without a home, he was glad to remain. Physical examination showed a thorax with flaring ribs and an increased anteroposterior diameter of the chest with hyperresonant percussion note and breath sounds somewhat distant. The teeth were in poor condition; blood-pressure, systolic 115 to 130, diastolic 75 to 90.

Experiment 113.—March 26, 1914. Basal metabolism. During the previous day the diet had contained 11.5 gm. KCl and a minimum of NaCl. The last meal at 6 p. m. had consisted of farina, 25; egg-white, 50; yolk, 50; sugar, 50; cream (20 per cent. fat), 60; KCl, 3.5 gm. Blood-pressure March 25, systolic, 140; diastolic, 95; just before the calorimeter experiment, systolic 135, diastolic 105.

L. C. M., laboratory helper, small frame, somewhat short and thin. He was born in Sicily where he lived until the age of 11. Shortly before leaving for this country he suffered from malaria, but since then has been in good health. For the last five years he has worked in the daytime and gone to school at night, consequently has taken but little exercise. Heart, lungs and abdomen normal.

Experiment 136.—May 4, 1914. Basal metabolism.

Experiment 137.—May 6, 1914. Between 9:50 and 9:53 drank a solution of 200 gm. C. P. dextrose in 400 c.c. water and 35 c.c. lemon juice. No glycosuria.

The subjects have been described in detail above and particular attention has been given to the athletic history, since the recent work in Benedict's laboratory (personal communication) has shown a difference in the metabolism of athletes and non-athletic individuals. From a study of the results in previous determinations of the normal metabolism one is led to suspect that a few distinctly abnormal cases have crept in. It has, therefore, been our practice to give the normal controls as careful physical examination as the patients. The importance of this is manifest if one considers that the onset of hyperthyroidism is usually accompanied by the symptoms of exuberant good health.

17. Cooke: Unpublished.

The details of the individual experiments are given below. The body weight at the start of the experiment is determined by weighing the subject shortly before he enters the calorimeter and then making the proper corrections for food, urine and insensible perspiration. All calculations are made from this weight, the surface area being reckoned from Meeh's[18] formula $12.312 \sqrt[3]{\text{WT}^2}$. Some actual determinations of the surface area of E. F. D. B. have shown that Meeh's formula is 14.3 per cent. too high in his case, while it is only 7.3 per cent. too high in the case of R. H. H. Calculated from a new formula, Meeh's figures are 14.5 per cent. too high in the case of G. L., 9.3 per cent. too high in the case F. C. G. and 13.4 per cent. too high in the case of L. C. M. These measurements will be given in detail in a subsequent paper. For purposes of uniformity, however, calculations are based on Meeh's formula, since this has been used in all other metabolism work. The work-adder was not attached to the calorimeter until May 16, 1913, and an exact record of the activity of the subjects was not obtained before this date. After the work-adder as described in Paper 2 was attached it was possible to compare the activity in different periods and in different experiments and express this in terms of the number of centimeters that the plummet was raised by the expansion of air within the box. The excursion of the plummet for certain movements of the subject was roughly calculated as follows: Raising arm to head, 0.3 cm.; lifting telephone to mouth, 4 cm.; turning from back to side, 7 cm.

In the tables the final calculations of calories per hour have been based on the indirect calorimetry as calculated from the oxygen consumption and the respiratory quotient. In the two experiments on F. C. G., where these were inaccurate the direct calorimetry was used, and in one of the hours in the experiment on G. L. where the CO_2 measurement was lost the non-protein R. Q. for the purposes of calculation was assumed to be 1.00.

In the experiments on E. F. D. B. on May 22 there was an evident error in the division of oxygen between the second and third and the fourth and fifth periods, so these were averaged in the final calculations

The methods of calculation have been described in Paper 1, but it may be well to remind the reader that the method of direct calorimetry represents the heat eliminated from the body, plus or minus the heat stored in or lost from the body, when the temperature of the body rises or falls. The calculation of the percentage of calories derived from protein, fat and carbohydrate is based on the urinary nitrogen and the non-protein respiratory quotient.

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18. Meeh: Oberflächenmessungen des menschlichen Körpers, Ztschr. f. Biol., 1879, xv, 425.

Subject Date	Weight Kg.	Period	End of Period	CO_2, Gm.	O_2 Gm.	R. Q.	H_2O, Gm.	Urine N Per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
G. L. 3/11/13	78.42	Preliminary	A. M. 9:50							
		1st Hr.	10:50	25.26	21.61	0.85	37.03	0.487	72.36	76.77
		2d Hr.	11:50	26.56	25.90	0.75	37.84	0.487	84.85	86.10
		1st Hr. P. C.	P. M. 12:50	29.61	28.57	0.75	37.88	0.404	94.12	87.75
		2d Hr. P. C.	1:50	.....	25.75	....	39.24	0.404	86.76*	92.53
		3d Hr. P. C.	2:50	30.33	23.44	0.94	38.98	0.404	80.86	95.67
E. F. D. B. 3/13/13	73.6	Preliminary	A. M. 9:35							
		1st Hr.	10:35	27.22	25.27	0.78	27.91	0.554	83.52	77.85
		2d Hr.	11:35	25.28	21.32	0.86	26.53	0.554	71.75	71.94
		1st Hr. P. C.	P. M. 12:35	29.51	23.58	0.91	31.19	0.621	80.27	84.87
		2d Hr. P. C.	1:35	31.12	25.50	0.89	30.50	0.621	86.42	82.87
		3d Hr. P. C.	2:35	30.30	24.94	0.88	30.40	0.621	84.41	81.46
		4th Hr. P. C.	3:35	29.92	24.10	0.90	32.02	0.621	81.92	86.02
E. F. D. B. 5/17/13	75.51	Preliminary	A. M. 9:30							
		1st Hr.	10:30	25.41	22.37	0.83	34.22	0.526	74.69	76.83
		2d Hr.	11:30	25.45	21.95	0.84	32.00	0.526	73.60	76.67
		3d Hr.	P. M. 12:30	25.00	21.24	0.86	30.68	0.526	71.41	74.13
E. F. D. B. 5/22/13	76.10	Preliminary	A. M. 9:30							
		2d Hr. P. C.	19:30	31.13	23.04	0.98	36.24	0.581	79.77	84.61
		3d Hr. P. C.	11:30	31.53	25.29	0.97	36.13	0.581	165.30	83.21
		4th Hr. P. C.	P. M. 12:30	32.45	22.49		35.07	0.581		83.91
		5th Hr. P. C.	1:30	31.95	28.84	0.95	36.63	0.581	162.04	84.45
		6th Hr. P. C.	2:30	29.73	18.18		36.78	0.581		84.96
E. F. D. B. 3/30/14	74.34	Preliminary	A. M. 11:25							
		1½ Hrs.	P. M. 12:55	36.10	32.26	0.81	45.08	0.518	107.30	113.13
		1½ Hrs.	2:25	37.58	34.88	0.78	46.48	0.518	115.24	113.14
E. F. D. B. 4/1/14	74.92	Preliminary	A. M. 11:27							
		2d Hr. P. C.	P. M. 12:27	27.47	24.30	0.82	30.51	0.856	80.50	81.65
		3d Hr. P. C.	1:27	29.66	26.17	0.83	31.75	0.830	86.91	81.50
		4th Hr. P. C.	2:27	28.13	25.35	0.81	32.87	0.900	83.60	85.98
		5th Hr. P. C.	3:27	28.83	25.89	0.81	33.39	0.577	86.11	82.76
		6th Hr. P. C.	4:27	27.12	23.86	0.83	32.98	0.577	79.61	83.63
E. F. D. B. 5/8/14	74.75	Preliminary	A. M. 11:05							
		2d Hr. P. C.	P. M. 12:05	30.55	23.41	0.95	32.59	0.604	80.53	76.35
		3d Hr. P. C.	1:05	30.91	24.28	0.93	33.55	0.604	83.08	79.08
		4th Hr. P. C.	2:05	29.37	22.49	0.95	32.48	0.604	77.33	75.63
		5th Hr. P. C.	3:05	30.28	22.06	1.00	32.22	0.604	76.47	76.46
E. F. D. B. 5/15/14	75.02	Preliminary	A. M. 10:50							
		2d Hr. P. C.	11:50	29.60	22.91	0.94	29.06	0.534	78.74	77.76
		3d Hr. P. C.	P. M. 12:50	31.35	22.12	1.03	30.02	0.534	77.26	80.09
		4th Hr. P. C.	1:50	31.07	24.04	0.94	30.73	0.534	82.67	80.28
		5th Hr. P. C.	2:50	29.95	22.21	0.98	30.87	0.534	76.96	79.99
		6th Hr. P. C.	3:50 A. M.	28.46	22.57	0.92	30.46	0.534	77.11	75.02

—Data in Hourly Periods

Direct Calorimetry Cal.	Rectal Temperature, C.	Av. Pulse	Work-Adder, Cm.	Non-Protein R. Q.	Per Cent. Calories from: Prot.	Fat	Carb.	Calories Per Hour: Per Kg.	Per Sq. M.	Remarks
	37.26									
78.95	37.30	..	....	0.87	18	37	46	0.92	32.07	Basal.
82.80	37.26	62	....	0.74	15	77	8	1.08	37.61	Basal.
94.21	37.28	88	....	0.75	11	77	12	1.20	41.72	At 11:63 a. m., 115 gm. commercial glucose.
86.54	37.20	..	....	....	12	..	..	1.11*	38.46*	
92.88	37.17	..	....	0.96	13	11	76	1.03	35.84	
	36.88									
78.09	36.90	..	....	0.78	18	62	20	1.13	38.63	Basal.
72.10	36.91	59	....	0.88	20	33	47	0.98	33.19	Basal.
87.12	36.84	67	....	0.94	21	16	63	1.10	37.13	At 11:38 a. m., 115 gm. commercial glucose.
83.46	36.87	64	....	0.91	19	25	56	1.18	39.97	
85.60	36.98	..	....	0.91	19	26	55	1.15	39.04	
84.64	36.99	60	....	0.93	20	19	61	1.11	37.89	
	36.96									
62.89	36.81	57	22	0.83	19	47	34	0.99	33.95	Basal.
77.00	36.80	55	13	0.85	19	41	40	0.97	33.45	Basal.
74.42	36.98	..	10	0.87	19	36	45	0.95	32.46	Basal.
	36.84									At 8:55 a. m., 230 gm. commercial glucose.
72.90	36.75	66	15	1.03	19	0	81	1.05	36.08	
82.51	26.84	53	17	1.02	19	0	81	1.09	37.38	
84.53	36.95	60	14							
82.50	37.01	58	16	0.99	19	2	79	1.07	36.64	
79.32	37.00	60	24							
	36.91									
110.72	36.88	54	30—	0.82	19	51	30	0.96	32.86	Basal.
116.62	36.99	56	37—	0.78	18	62	20	1.03	35.29	Basal.
	36.84									At 9:54 a. m., protein meal (10.5 gm. N).
84.05	36.91	57	24—	0.83	28	42	30	1.07	36.79	
77.92	36.89	57	28—	0.83	25	43	32	1.16	39.72	
86.71	36.93	58	30—	0.81	29	46	25	1.12	38.21	
81.62	36.94	57	26—	0.81	18	53	29	1.15	39.36	
88.88	37.04	58	33—	0.83	19	46	35	1.06	36.39	
	36.66									
75.09	36.67	61	14.1	0.99	20	3	77	1.08	36.86	At 10:05-10:07 a. m., 200 gm. dextrose.
83.22	36.78	61	23.5	0.96	19	11	70	1.11	38.02	
73.61	36.78	61	18.8	0.99	21	2	77	1.03	35.39	
76.05	36.79	62	26.0	1.06	21	..	79	1.02	35.00	
	36.69									
78.83	36.73	55	19.6	0.97	18	8	74	1.05	35.95	At 9:50-9:53 a. m., 200 gm. dextrose.
78.30	36.73	58	22.5	1.09	18	..	82	1.03	35.28	
79.13	36.73	59	33.1	0.97	17	8	75	1.10	37.75	(Carbohydrate breakfast at 6:15 a. m.).
81.32	36.76	59	21.8	1.03	18	..	82	1.03	35.14	
72.36	36.74	57	34.0	0.95	18	15	67	1.03	35.21	

* Estimated from CO_2.

TABLE 2.—

Subject Date	Weight Kg.	Period	End of Period	CO_2, Gm.	O_2 Gm.	R. Q.	H_2O, Gm.	Urine N Per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.
E. F. D. B. 5/18/14	73.70	Preliminary	10:50							
		1st Hr.	11:50	23.92	21.08	0.83	28.03	0.530	70.29	67.48
		2d Hr.	P. M. 12:50	23.85	21.88	0.79	28.08	0.530	72.38	69.37
F. C. G. ... 3/17/13	56.5	Preliminary	A. M. 9:02							
		1st Hr.	10:02	22.80	.....	....	17.77	0.491	.....	54.43
		2d Hr.	11:02	22.92	.....	....	19.69	0.491	.....	59.16
		3d Hr.	P. M. 12:02	22.59	.....	....	20.90	0.491	.....	60.70
F. C. G. ... 3/17/13	56.5	Preliminary	1:00							
		2d Hr. P. C.	2:00	14.86	41.52	0.85	23.05	0.491	139.35	60.85
		3d Hr. P. C.	3:00	23.53	21.08		30.51	0.491		68.89
		4th Hr. P. C.	4:00	22.73	25.27	0.78	26.08	0.491	69.59	62.52
F. C. G. ... 4/22/13	54.82	Preliminary	A. M. 9:45							
		1st Hr.	10:45	21.92	.....	....	25.40	.....	.....	58.96
		2d Hr.	11:45	22.05	.....	....	26.85	.....	.....	61.94
		3d Hr.	P. M. 12:45	21.08	.....	....	26.26	.....	.....	62.60
		4th Hr.	1:45	21.86	.....	....	28.59	.....	.....	63.33
		5th Hr.	2:45	22.03	.....	....	30.09	.....	.....	68.43
R. H. H. ... 3/19/13	62.00	Preliminary	A. M. 9:42							
		1st Hr.	10:42	26.15	21.59	0.88	27.90	.....	73.54	66.50
		2d Hr.	11:42	27.42	20.98	0.95	28.93	.....	72.78	69.27
Louis M. ... 3/26/13	51.70	Preliminary	A. M. 10:10							
		1st Hr.	11:10	20.53	18.73	0.80	28.92	0.522	61.91	64.64
		2d Hr.	P. M. 12:10	19.95	17.40	0.83	26.95	0.522	57.99	64.44
		3d Hr.	1:10	22.44	20.07	0.81	28.10	0.522	66.57	71.00
		4th Hr.	2:10	18.34	18.05	0.74	25.73	0.522	58.71	66.51
		5th Hr.	3:10	22.13	20.71	0.78	27.36	0.522	68.20	68.38
		6th Hr.	4:10	19.36	19.23	0.73	25.85	0.522	62.51	67.86
Louis M. ... 3/28/13	53.49	Preliminary	A. M. 11:14							
		3d Hr. P. C.	P. M. 12:14	23.43	22.62	0.75	24.08	0.703	73.76	64.89
		4th Hr. P. C.	1:14	24.27	22.67	0.78	29.15	0.695	74.44	75.48
		5th Hr. P. C.	2:14	26.84	25.11	0.78	34.80	0.970	82.02	79.07
		6th Hr. P. C.	3:14	26.44	25.11	0.77	34.38	1.014	81.70	77.18
		7th Hr. P. C.	4:14	24.85	23.21	0.78	35.42	1.138	75.38	83.35
		8th Hr. P. C.	5:14	26.25	24.79	0.77	34.71	1.112	80.53	81.28
John L. 3/26/14	70.94	Preliminary	A. M. 11:20							
		1st Hr.	P. M. 12:20	21.12	19.51	0.79	25.77	0.363	64.65	66.00
		2d Hr.	1:20	21.37	19.62	0.79	24.56	0.363	65.10	68.26
		3d Hr.	2:20	21.07	19.97	0.77	24.01	0.363	65.85	66.72
L. C. M. .. 5/4/14	59.50	Preliminary	A. M. 11:02							
		1st Hr.	P. M. 12:02	22.39	20.71	0.79	28.32	0.534	68.34	71.73
		2d Hr.	1:02	22.14	18.98	0.85	27.28	0.534	63.57	70.36
L. C. M. .. 5/6/14	60.98	Preliminary	A. M. 10:52							
		2d Hr. P. C.	11:52	29.94	23.73	0.92	33.43	0.578	81.05	73.19
		3d Hr. P. C.	P. M. 12:52	30.30	22.03	1.00	32.38	0.578	76.46	74.95
		4th Hr. P. C.	1:52	30.65	21.90	1.02	32.94	0.578	76.21	77.37

—(Continued)

Direct Calorimetry Cal.	Rectal Temperature, C.	Av. Pulse	Work-Adder, Cm.	Non-Protein R. Q.	Per Cent. Calories from Prot.	Fat	Carb.	Calories Per Hour Per Kg.	Per Sq. M.	Remarks
	36.76									
67.14	36.76	57	9.8	0.83	20	46	34	0.95	32.48	Basal.
70.23	36.78	67	18.2	0.79	19	58	23	0.98	33.45	
	37.03									
58.83	37.15	..	....	....	..	..	..	1.04	30.75	Basal. Profound sleep during second and third periods. O_2 leak.
55.75	37.11	..	....	....	..	..	..	0.99	32.45	
56.99	37.06	..	....	....	..	..	..	1.01	31.43	
	37.02									
66.85	37.17	..	....	0.86	19	39	42	1.18	36.87	At 12 m., plate of oatmeal. O_2 leak.
60.53	37.00	..	....					1.07	33.39	
60.83	36.95	..	....	0.78	19	61	20	1.08	33.59	
	37.04									
57.28	37.03	74	....	....	..	..	..	1.04	32.22	Basal. O_2 leak.
62.68	37.07	68	....	....	..	..	..	1.14	35.25	
60.60	37.04	64	....	....	..	..	..	1.10	34.08	
58.15	36.94	66	....	....	..	..	..	1.06	32.71	
64.88	36.87	70	....	....	..	..	..	1.18	36.49	
	36.76									
69.22	36.82	..	....	....	..	..	..	1.19	38.12	Basal. Urine not obtained.
70.31	36.85	..	....	....	..	..	..	1.19	37.73	
	37.18									
58.39	37.07	..	....	0.80	22	56	24	1.20	36.23	Basal.
61.88	37.04	..	....	0.84	24	40	36	1.12	33.92	
75.26	37.15	..	....	0.82	21	49	30	1.29	38.95	
59.27	37.00	..	....	0.72	24	73	3	1.14	34.35	
70.95	37.08	..	....	0.77	20	63	17	1.32	39.91	
62.47	36.98	..	....	0.71	22	77	1	1.21	36.58	
	37.10									
74.89	37.28	..	....	0.74	25	68	7	1.39	42.20	8:25-9:25 a. m., 725 gm. chopped beef = 23.93 gm. N + 100 gm. fat.
81.49	37.43	..	....	0.77	25	59	16	1.40	42.59	
74.67	37.36	..	....	0.76	31	55	14	1.54	46.92	
78.43	37.41	..	....	0.75	33	58	9	1.54	46.74	
80.09	37.38	..	....	0.76	40	49	11	1.42	43.12	
81.96	37.39	..	....	0.75	37	54	9	1.51	46.07	
	37.11									
52.70	36.89	61	13.0+	0.78	15	62	23	0.91	30.64	Basal.
68.56	36.94	55	13.0+	0.79	15	61	24	0.92	30.85	
62.04	36.88	57	38.7	0.76	15	69	16	0.92	31.21	
	36.94									
66.95	36.85	74	22.0+	0.78	21	59	20	1.15	36.41	Basal.
73.48	36.92	70	18.2	0.86	22	37	41	1.07	33.87	
	36.84									
65.74	36.70	85	19.1	0.95	19	15	66	1.33	42.48	9:50-9:53 a. m., dextrose, 200 gm.
73.60	36.68	82	30.1	1.06	20	..	80	1.25	40.07	
82.50	36.79	79	38.2	1.08	20	..	80	1.25	39.94	

The results are expressed in terms of grams and calories per hour, since this is the length of period used in the Cornell and Sage calorimeters and is the nearest unit of the length of the actual experimental period used in most of the modern machines.

DISCUSSION OF RESULTS

As explained in Paper 1 of this series, the determination of the heat production by the methods of direct and indirect calorimetry have been found to give identical results in the work of Rubner, Atwater and Benedict, Lusk and his coworkers. Rubner demonstrated this on the dog in long periods, Atwater and Benedict on man at rest and at work, Lusk on dogs in hourly periods and Howland, in Lusk's laboratory, on babies both normal and atrophic. To this list may be added the work of Armsby[19] on cattle in twenty-four-hour experiments and the work of Carpenter and Murlin[20] who studied the metabolism of women before and after confinement, in Benedict's laboratory. A comparison of the figures for direct and indirect calorimetry obtained in Benedict's calorimeter shows excellent agreement in the two- and three-hour periods. Out of a total of twenty-eight periods, the two methods were within 5 per cent. of each other in seventeen, while only six showed a disagreement over 10 per cent.

Table 3 gives in parallel columns the calories in each of our experiments as measured by the methods of direct and indirect calorimetry. The totals of all the experiments show that the two methods come within 0.17 per cent. of each other. Even when we consider periods as short as one hour, the agreement may be striking. On the normal control, E. F. D. B., there were a total of 26 one-hour periods. In 17 of these the methods of direct and indirect calorimetry agreed within 5 per cent., in 6 periods within 6 to 9 per cent., while three isolated periods showed a disagreement of 11, 12 and 16 per cent., respectively. Work with the Sage calorimeter on normal controls and on patients with a large variety of diseases has shown that in a total measurement of 27,632 calories the direct calorimetry gives a figure only 1.62 per cent. lower than the indirect. There is, therefore, no reason to believe that in long periods, or in the average of a number of short periods, there is any essential difference between the two methods. As will be shown later, there is good reason to believe that indirect calorimetry gives the more accurate results in short periods.

There are two methods of calculating the indirect calorimetry, both of which involve factors that change with the respiratory quotient.

19. Armsby: Food as Body Fuel, Pennsylvania State College Agricultural Experiment Station, Bull. 126.

20. Carpenter and Murlin: The Energy Metabolism of Mother and Child Just Before and Just After Birth, The Archives Int. Med., 1911, vii, 184.

TABLE 3.—SUMMARY OF RESULTS. AVERAGES OF PERIODS

Subject	Date	Weight at Start, Kg.	Square Meters Body Surface (Meeh)	Calories per Sq. M. per Hour	Variation from Average Normal Basal 34.7	Per Cent. Rise above Subject's Own Basal Metabolism	Average R. Q.	Total Calories Measured in Each Experiment: Method of Indirect Calorimetry	Total Calories Measured in Each Experiment: Method of Direct Calorimetry Rectal Temp.	Method of Direct Calorimetry Surface Temperature	Character of Experiment
G. L.	3/11/13	78.42	2.256	34.84	+ 0	..	0.80	157.40	161.75	......	Two basal hours.
	3/11/13	78.42	2.256	38.67	....	11	....	261.54	273.63	......	First three hours after 115 Comm. glucose = 100 C. P. dextrose
E. F. D. B.	3/13/13	73.6	2.162	35.91	+ 3	..	0.82	155.27	149.79	......	Two basal hours.
	3/13/13	73.6	2.162	38.51	....	7	0.90	333.02	341.22	......	First three hours after 115 Comm. glucose = 100 C. P. dextrose
	5/17/13	76.51	2.200	33.29	— 4	..	0.84	219.70	214.31	......	Three basal hours.
	6/22/13	76.10	2.211	36.82	....	11	0.97	407.11	401.96	......	1½ to 5½ hours after 230 Comm. glucose = 200 C. P. dextrose.
	3/30/13	74.34	2.177	34.08	— 2	..	0.80	222.50	227.34	232.23	Three basal hours.
	4/ 1/13	74.92	2.188	38.09	....	12	0.82	416.75	419.18	413.58	1½ to 6½ hours after protein meal (10.5 gm. N).
	6/ 8/13	74.75	2.185	36.32	....	10	0.96	317.41	307.97	317.60	1 to 5 hours after 200 C. P. dextrose.
	5/15/13	75.02	2.190	35.87	....	9	0.96	392.74	389.94	395.82	1 to 6 hours after 200 C. P. dextrose taken 3½ hours after breakfast
	5/18/13	73.70	2.164	32.97	— 5	..	0.81	142.67	137.37	138.33	Two basal hours.
F. C. G. ..	3/17/13	56.5	1.313	31.54	— 9	..	....	*	......	......	Three basal hours.
	3/17/13	56.5	1.813	34.60	....	10	....	*	......	......	1 to 4 hours after breakfast of protein 13.1, fat 10.2, carbohydrate 35.5
	4/22/13	54.82	1.778	34.15	— 2	....	....	146.32	139.53	......	Five hours basal.
R. H. H. ..	3/19/13	62.00	1.929	37.93	+ 9	..	0.92	146.32	139.53	......	Two hours basal.
Louis M. ..	3/26/13	51.70	1.709	36.66	+ 6	..	0.78	375.89	388.22	......	Six hours basal.
	3/28/13	53.49	1.748	44.61	....	22	0.77	467.83	471.53	......	2 to 8 hours after 725 gm. beef = 23.93 N and 100 fat
John L. ..	3/26/14	70.94	2.110	30.90	—11	..	0.78	195.60	183.30	188.50	Three hours basal.
L. C. M. ..	5/ 4/14	69.50	1.887	35.14	+ 1	..	0.82	131.91	140.43	141.73	Two hours basal.
	6/ 6/14	60.98	1.908	40.83	....	16	0.98	233.71	221.93	225.28	1 to 4 hours after 200 gm. C. P. dextrose.
Total								4577.37	4569.40		....

* Oxygen figures discarded on account of leaks.

The first is the standard method of Zuntz and his associates, based on the liters of oxygen consumed, which are multiplied by a factor that increases about 8 per cent. as the quotient rises from 0.72 to 0.97. The second method is based on the liters of CO_2 produced, the figure for which is multiplied by a factor which decreases 24 per cent. as the

TABLE 4.—HEAT PRODUCTION OF NORMAL MEN, AGES 20 TO 50. COMPARISON OF CALORIES PER KILOGRAM AND PER SQUARE METER

Subject	Weight, Kg.	Calories per Kilogram per Hour	Calories per Sq. Meter per Hour	Percentage Variation from Average		Calories per Sq. Meter per Hour According to New Surface Area Formula	Per Cent. Variation from Average
				Calories per Kg.	Calories per Sq. Meter		
F. G. B.*.....	83.0	1.01	35.8	— 4	+ 5	....	...
G. L.	78.4	1.00	34.8	— 5	+ 2	40.7	+2
F. A. R.*.....	74.3	0.95	32.4	— 9	— 5	....	...
E. F. D. B. ..	74.3	1.00	34.1	— 5	0	39.8	—0
John L.	70.9	0.92	30.9	—12	—10	....	...
J. J. C.*......	67.6	0.96	31.7	— 8	— 7	....	...
J. R.*..........	66.0	1.00	32.8	— 5	— 4	....	...
R. H. H.	62.0	1.18	37.9	+14	+11	40.9	+3
L. C. M.	59.5	1.11	35.1	+ 6	+ 3	40.5	+2
F. C. G.	54.8	1.10	34.2	+ 5	0	37.7	—5
Louis M.	51.7	1.21	36.7	+16	+ 7	....	...
T. M. C.*.....	49.0	1.13	33.8	+ 8	— 1	....	...
Average	....	1.05	34.2	± 8.1	± 4.6	39.9	±2.4
79 normal men in groups† 8 weights....	75-85	1.01	35.2	— 7	+ 2	....	...
20 weights....	65-75	1.02	34.1	— 6	— 2	....	...
41 weights....	55-65	1.09	34.7	+ 1	0	....	...
10 weights....	45-55	1.18	35.5	+ 9	+ 2	....	...
Average	.....	1.08	34.7	± 5.8	± 1.5	....	...

* Determinations made by Benedict and Joslin.[29]
† Taken largely from work of Benedict, Emmes, Roth and Smith.[10]

quotient rises from 0.72 to 0.97. Tables for this latter calculation are given by Benedict and Talbot,[21] who prefer this method in using an apparatus in which they consider that for short periods the determination of the carbon dioxid is more exact than the determination of

21. Benedict and Talbot: Studies in the Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1; The Gaseous Metabolism of Infants, Carnegie Institution of Washington, Pub. 201.

oxygen. It is true that in the closed circuit type of apparatus the measurement of the oxygen is subject to many corrections for changes in the barometer, temperature, moisture, etc., and that it is liable to a plus error in the case of leaks. This error affects the quotient and produces such a change in the CO_2 factor that one usually obtains better results by basing the calculations on the oxygen. This is brought out clearly in Table 5, which gives a comparison of the methods of calculating the heat production from the oxygen and from the CO_2, showing the errors in the results arising from various assumed errors in the measurements. It will be noted that in the great majority of the cases

TABLE 5.—COMPARISON OF METHODS OF CALCULATION WITH ASSUMED ERRORS IN MEASUREMENT OF CO_2 AND O_2

CO_2		O_2		R.Q.	Calorific Value 1 Liter of CO_2		Calorific Value 1 Liter of O_2		Indirect Calorimetry Based on CO_2		Indirect Calorimetry Based on O_2	
Liters	Assumed Error %	Liters	Assumed Error %		Cal.	Per Cent. Change	Cal.	Per Cent. Change	Cal.	Per Cent. Error	Cal.	Per Cent. Error
12.94	0	15.64	0	0.83	5.829	.....	4.807	.....	75.40	.....	75.17	.....
12.94	0	17.20	+10	0.75	6.319	+8.4	4.708	−2.1	81.74	+8.4	80.98	+7.7
14.23	+10	15.64	0	0.91	5.424	−7.0	4.904	+2.0	77.18	+2.4	76.70	+2.0
12.94	0	16.42	+5	0.79	6.062	+4.0	4.758	−1.1	78.44	+4.0	78.13	+3.9
13.59	+5	15.64	0	0.87	5.617	−3.6	4.855	+1.0	76.33	+1.2	75.93	+1.0
12.29	−5	16.42	+5	0.75	6.319	+8.4	4.708	−2.1	77.66	+3.0	77.31	+2.8
13.59	+5	14.86	−5	0.91	5.424	−7.0	4.904	+2.0	73.71	−2.2	72.87	−3.1
12.94	0	14.86	−5	0.87	5.617	−3.7	4.855	+1.0	72.68	−3.6	72.15	−4.0

cited the error from the use of the oxygen factor is smaller than that from the CO_2. Even with a plus error of 5 to 10 per cent. in the oxygen and no error in the CO_2, the results obtained by using the oxygen are the better, since the minus change in this factor compensates for part of the error. In the two instances shown, in which the results obtained by the use of the CO_2 factor are closer to the theory than those obtained by the use of the oxygen factor, it will be noted that there is a minus error in the oxygen. This is the least frequent of all the errors.

Many investigators in seeking for an index of the heat production express the results in grams or cubic centimeters of CO_2, and compare the elimination of this gas in different individuals, apparently with the impression that they are comparing the actual total metabolism. As we have seen above, a man eliminating, say, 3.13 c.c. CO_2 per kg. per min-

ute might have a heat production 24 per cent. higher than another man eliminating the same amount of CO_2 whose respiratory quotient was at the other end of the scale. If one uses the oxygen consumption the possible error from this source is diminished to 8 per cent. Since it is such an easy calculation to determine the actual calories by using the oxygen figure and the respiratory quotient, it seems inexcusable to leave the results at a stage which might give false impressions. It is only in special investigations on the ventilation of the lungs, etc., that the amounts of the gases themselves are of any direct interest. In most experiments it is the actual calories that need to be determined.

Experience has shown that with careful technic the indirect calorimetry in hourly periods remains fairly uniform in fasting experiments and shows regular curves in experiments after food. The direct calorimetry in hourly periods is a matter of greater technical difficulty on account of the fact that the human body is poorly constructed for accurate thermal measurements. As was shown in Paper 1, a rise or fall of 1 degree centigrade in the average temperature of the body means a storage or loss of about 58 calories if the man weighs 70 kilograms. This is based on the assumption that the specific heat of the body is 0.83, a figure which has been accepted for many decades, although without satisfactory experimental support. Rubner[22] has found that the specific heat of lean flesh is 0.828, of fatty tissue 0.53 and of pure fat 0.45. Rosenthal[23] at an earlier date had made the following determinations: compact bone 0.30, spongy bone 0.710, defibrinated blood 0.927, dried muscle 0.330. Using these figures and the figures for the average composition of the body as given by Vierort[24] one obtains a specific heat of approximately 0.77. A body rich in fat would, of course, approach the figure 0.45 and one rich in water would approach 1.00. Theoretically, one should change the specific heat each time a subject drinks water or voids. This latter would be a matter of small importance, but in the case of a very obese person one-half of whose weight consisted of fat, the true specific heat would not be far from 0.64.

In normal subjects the temperature changes in hourly periods are small and according to the work of Benedict and Slack,[25] the temper-

22. Rubner: Kalorimetrie, Tigerstedt's Handbuch der physiologische Methoden, i, 170.

23. Rosenthal: Ueber die specifische Wärme thierische Gewebe, Arch. f. Physiol., 1878, p. 215.

24. Vierort: Daten und Tabellen. Jena, 1893, p. 249.

25. Benedict and Slack: A Comparative Study of the Temperature Fluctuation in Different Parts of the Human Body. Carnegie Institution of Washington, 1911, Pub. 155.

ature curves in different parts of the body are nearly parallel. Lusk[26] and his coworkers did not find this to be the case in the dog after the ingestion of large amounts of food since this caused a greater rise in surface than in rectal temperature. When one considers the mechanism of the regulation of body temperature in fever it becomes evident that the rise in surface temperature follows that of the internal temperature. Every clinician has felt in some patients, particularly those seriously ill, the extremities growing colder and colder while the internal temperature is rising and, conversely, has felt the surface grow warmer while the temperature is falling, demonstrating the fact that the two are not always parallel.

It was on account of these considerations that the surface thermometers described in Paper 2 were used after May, 1913, the two units of the surface thermometer being strapped over the right and left pectoralis major as near as possible to the heart and dome of the liver. They were covered with a thick layer of cotton in an effort to obtain the temperature of the subcutaneous tissue rather than that of the naked skin. After March 12, 1914, a second surface thermometer was added and its two units placed in various parts of the anterior surface of the thorax and abdomen and also in the axillae. The results have been confusing and difficult to interpret, but they have indicated clearly that the different parts of the body do not show parallel temperature curves. A fruitless search has been made for some part of the body which will give a true index of the mean temperature change. In the majority of all the experiments the rectal temperature was the more satisfactory, but in typhoid fever the surface gave better results. The method of investigation was as follows:

In a total of eighty-five experiments satisfactory rectal and surface temperature measurements were made. Twenty-eight of these experiments were on typhoid fever patients. For the reasons above stated the heat production as determined by the method of indirect calorimetry was considered to be the true heat production, and the results of the direct calorimetry as calculated by three different methods were compared with this as shown in the table below. In all three methods the figure for the heat eliminated from the body was, of course, the same. To obtain the heat produced, the heat stored in or lost from the body, as determined by each of the two measurements, and by a mean of the two, has been added to or subtracted from the heat eliminated.

It will be seen from Table 6 that in the total of 85 experiments the rectal temperature gave the best results, approximating the theoretical more closely than either of its competitors in 36 cases, coming within 5

26. Williams, Riche and Lusk: Metabolism of the Dog Following the Ingestion of Meat in Large Quantity, Jour. Biol. Chem., 1912, xii, 349.

per cent. in 62 cases and involving a total error of only 0.90 per cent. While the surface temperature gave the best results in 24 cases, it showed an error of over 15 per cent. in 5 cases and did not prove as reliable as the mean of surface and rectal. In typhoid fever the honors were more evently divided and all three methods gave surprisingly good results in spite of the large changes in body temperature sometimes encountered. The surface temperature alone gave the best results in 13 of the 28 experiments and also the lowest total error.

TABLE 6.—Comparison of Surface and Rectal Temperatures as an Index of Average Body Temperature; Percentage Differences between Indirect Calorimetry and Direct Calorimetry Calculated According to Three Methods

Percentage Difference in Individual Experiments	Number of Experiments Falling in Each Group					
	Twenty-Eight Typhoid Experiments			Eighty-Five Experiments in Various Diseases, Including the Twenty-Eight Typhoid Observations		
	Rectal Temperature Alone	Surface Temperature Alone	One-half Rectal, One-half Surface	Rectal Temperature Alone	Surface Temperature Alone	One-half Rectal, One-half Surface
0 to 5	18	18	18	62	41	53
5 to 10	9	9	10	19	28	27
10 to 15	1	1	0	4	11	4
15+	0	0	0	0	5	1
Total difference	—1.32	—1.17	—1.24	—0.90	—1.46	—1.18
Number giving results nearest to indirect	8	13	7	46	24	15

As a result of the above analysis the rectal temperature has been adopted as the standard indicator of the average body change in hourly periods, but with a full realization of its limitations. In many experiments, particularly in those with rapidly changing temperature, better results would be obtained by using the surface temperature, but surface thermometers are more easily displaced than rectal and are not so reliable in the long run. Theoretically, one would obtain the best results by the use of many thermometers placed in the rectum, axillae, groin, on the surface of the body in many areas, giving each measurement an estimated weight, and then calculating the mean temperature change. Our attempt to do this in a small way by giving the rectal and surface equal weights did not lead to better results. For many reasons it seems advisable to attach as little apparatus as possible to the subject, and it is

doubtful if the use of many thermometers at one time will ever become a standard method.

There may be several reasons why these results are not in accord with the conclusion of Benedict and Slack. Working with normal subjects who showed comparatively small fluctuations in body temperature, they made many measurements at different depths in the rectum and vagina and found that while there was a sharp fall in temperature between a point 7 cm. within the rectum and a point just within the anus, nevertheless the temperature of points at different depths remained parallel, though at a different level. Temperatures taken in the well-closed axilla and groin were also parallel with the rectal. The mouth was found to be an unsatisfactory place to obtain the mean body temperature. Considerable difficulty was experienced in obtaining satisfactory measurements of the surface of the body and of the hands, and the writers speak of the difficulty of devising a thermometer that will be shielded so that it may assume the body temperature and yet not interfere with the natural liberation of heat.

As we have mentioned above, our surface thermometers were covered with a thick layer of cotton wool and represented a subcutaneous rather than a surface measurement, and therefore not comparable to the axillary, groin and shallow rectal measurements of Benedict and Slack. All of the latter are in the neighborhood of large blood-vessels and might be expected to rise and fall simultaneously.

All of this brings us back to the desirability of using the method of indirect calorimetry as the standard and checking its accuracy by the level of the respiratory quotient and the agreement with the direct calorimetry. All the evidence of this laboratory shows that the quotient rises and falls in regular curves in rest experiments when hourly periods are used. If, therefore, in any experiment the quotient shows a variation not accounted for by recent food, we suspect an error and usually find it compensated for in the next period. This error is almost always found in the calculation of the residual oxygen in the box at the close of the hour. Luckily there is an automatic correction in the method of calculating the indirect calorimetry. If in the first hour the oxygen estimation be too high, the quotient will be too low, and consequently the factor by which the oxygen is multiplied will be diminished. In the second hour when the error has been compensated for, the oxygen estimation will be too low, the quotient too high and the factor increased. This is another reason why the indirect calorimetry is more reliable than the oxygen consumption as an index of metabolism.

The method of direct calorimetry serves as an invaluable check, and if in any two- or three-hour experiment during which the body

temperature changes less than half a degree, the methods of indirect and direct calorimetry do not agree within 5 per cent., one should suspect a defect in the calorimeter. If in the next experiment a similar divergence be found, an alcohol check should be made and the error located. If one can prove that the error was due to any one particular determination, all calculations affected by this must be rejected as in the two experiments on F. C. G. It is by no means necessary to reject the results of the method of calorimetry not affected by the error. There is only one determination that enters into both methods of calculation, but an error in this would cause the two methods to diverge and not to err in the same direction. If through gross carelessness the first sulphuric acid bottle were allowed to gain so much weight that water vapor passed by into the CO_2 absorber, the direct calorimetry would be too low and the indirect too high, since both the quotient and the oxygen factor would be increased.

DETERMINATION OF THE AVERAGE NORMAL

The selection of the proper normal base line is a matter of extreme difficulty. It is also a matter of prime importance in determining whether or not a patient or group of patients shows a total metabolism which is above or below the normal limits. In dealing with patients suffering from acute diseases it is sometimes possible to wait until the patient recovers completely and then determine his normal heat production. This is not always practicable and even when it can be done one has no guarantee that the metabolism has returned to normal unless several measurements at considerable intervals be made. In the case of patients with chronic diseases this method is out of the question. The method most commonly used is that of selecting groups of normal controls to correspond as nearly as possible to each individual patient. This of course is the ideal method if many controls be selected, but it is extremely doubtful if any investigator up to the present date has been able to gather enough satisfactory controls for each patient. The recent work of Benedict, Emmes, Roth and Smith[10] may remedy this, on account of the large number of individuals whose metabolism was determined. Even with this wealth of material one may err if allowed to pick out a small group. The individual variation is large, as one can see from a careful study of the figures. It is, perhaps, unfair to draw many deductions before the full description of the subjects is published, but we may rely on the statement that all were in presumably good health. The average heat production of the 89 men was 833 calories per square meter per day or 34.7 calories per square meter per hour. The average heat production of the 12 men studied in the bed calorimeters and grouped in Table 4 was 34.2 calories

per square meter per hour. This striking agreement is another proof that the Benedict universal respiration apparatus gives results which are almost identical with the calorimeter. For this reason the 7 subjects examined by us have for purposes of calculation been grouped with the 89 of Benedict, Emmes, Roth and Smith. In order to rule out those who were distinctly over- or underweight, the subjects were all plotted in a curve, the height forming the abscissa and the weight the ordinates. All but 9 of the subjects could be grouped between two lines not very far apart. Of the 9, W. S., O. F. M., Prof. C., H. F., F. E. M. and F. A. R. were evidently much heavier in proportion to their height than their fellows, and for this reason excluded from the averages. It is interesting to note that their average heat production was 31.5 calories per square meter. Two of the 9, R. A. C. and B. N. C., were evidently very light in proportion to their height. E. P. C. came just outside the line, but so close to it that he has not been excluded from the averages. All those over 50 years of age were arbitrarily excluded and also those under 20 years. To the remaining 72 were added the normal controls of the present paper. This process of exclusion and addition left a fairly homogeneous total of 79 whose average metabolism was 34.7 calories per square meter per hour, or exactly the same as that of the original 89 before the addition of 7 and the exclusion of 17. These 79 have been divided into four groups according to body weight in Table 4.

If we plot the heat production of all the subjects according to surface area, the range of individual variation becomes apparent. Of the total 79 we find 40 within 5 per cent. of the base line drawn at the average figure 34.7, 28 are from 5 to 10 per cent. from the average and 11 are more than 10 per cent. from the average. Of these, 6 were between 10 and 14 per cent. above, and 5 were between 10 and 15 per cent. below. This means that when we speak of a normal average we must remember a normal variation of at least 10 per cent. above and below and realize that in about 14 per cent. of the normal men the variation may be plus or minus 10 to 15 per cent. One cannot help but feel that most of the cases showing a variation of more than 10 per cent. from the average will be found to present some distinct cause for the unusual metabolism, such as an unusual degree of muscular development or muscular disuse or an unsuspected disturbance of the thyroid secretion, or the mild infection with tuberculosis which all of us pass through at some time in our lives. At any rate, one can be fairly certain that if the total heat production be 15 per cent. from the average it is distinctly abnormal, and if it be more than 10 per cent. from the average it must be regarded with great suspicion.

It may be argued that some of the variation may be due to differences in body weight. If we study the 24 normal subjects in the table we have been considering, whose weights are between 60 and 65 kg., the same variation is apparent. Of the 24, only 13 are within 5 per cent. of the average, 5 are between 5 and 12 per cent. above and 6 are from 5 to 10 per cent. below. If one investigator chanced to select this last group of 6 for his controls his average would be about 15 per cent. lower than if he selected the group of 5 cases with high metabolism. This of course is an extreme instance. It may still be argued that the factor of height must be considered. In the same table we find an exceedingly homogeneous group of 7 men whose weights are between 60.1 and 60.5 kg. and whose heights are between 171 and 175 cm. Even in this group there is a difference of 13 per cent. between the highest and the lowest and a difference of 9 per cent. between the averages of the highest 4 and the lowest 3 in this group.

This somewhat lengthy discussion is intended to show the chances of serious error in selecting any small group of normal controls to compare with a pathological case. One cannot say just how large the group should be, but it is safe to say that it must exceed 5, should exceed 10 and if possible, 50. It is obviously much better to use all the normal controls so far studied and let personal selection play no part. This can be done by basing all comparisons on the average heat production per square meter of body surface.

In Table 4 we find a comparison of the heat production calculated according to surface area and according to weight. A study of the percentage variation from the average shows clearly that all four weight groups are within 2 per cent. of the mean heat production per square meter of body surface. In other words, one can determine the average normal by this method by using a group of individuals of any weight within ordinary limits. On the other hand, the figures per kilogram of body weight show the customary diminution as weight increases and there is a difference of 16 per cent. between the heavy group and the light group. In other words, there is no such thing as an average calories per kilogram for normal men, but only a normal average for each weight. To find the normal for a given man by this method one must consult a curve. To find the normal for a given man by the method of surface area one needs only to remember the figure 34.7.

Shortly after the experimental work on the normal controls was completed it seemed advisable to investigate the accuracy of Meeh's formula and if possible devise a new formula which could be applied to individuals who depart materially from the average body form. Five subjects were measured and it was found that there was a con-

sistent plus error in Meeh's formula which, in the case of a very fat woman, amounted to 36 per cent. In two of the normal controls whose heat production had been determined, the surface area was actually measured and the errors in Meeh's formula were found to be as follows: E. F. D. B., + 14 per cent., R. H. H., + 7 per cent. In three others, G. L., F. C. G. and L. C. M., the surface area was calculated by the new formula and found to be, respectively, 14.5 per cent., 9.3 per cent. and 13.4 per cent. lower than the results obtained by Meeh's formula. Since in all four cases the new surface area figures are lower than the old results obtained from Meeh's formula, the heat production per square meter of body surface, according to the new formula, would be about 7 to 15 per cent. higher, the average being 39.9. As will be seen in the last two columns of Table 3, the new results are somewhat more uniform than the old results, but are on a higher level, and it is quite possible that it may be necessary to adopt a higher normal average than 34.7. The general principle of Meeh's formula seems to be correct for individuals of average shape, and for this reason it may be used as the standard in large groups of subjects. In the case of very fat individuals, Meeh's formula would give a figure for the calories per square meter which would be much too low. It seems probable that some of the variations from the average normal figure per square meter can be explained by the variable error in the old formula. Future use of the new formula will, it is hoped, clear up this point. The details of the new method will appear in the following paper.

There is but little evidence against Rubner's law that metabolism is proportional to surface area. As we have seen there is a plus error in Meeh's formula for determining surface area. Nevertheless, in a group of normal men of approximately average build between the weights of 45 and 85 kilograms the metabolism is, on the whole, proportional to the surface area as determined by Meeh's formula. When we come to extend Rubner's law to babies and dogs studied in the modern types of apparatus with the modern scrupulous care to exclude the effect of muscular work, we find the figure for the calories per square meter changed, yet not nearly so much changed as the figure for the calories per kilogram of body weight. Murlin and Hoobler[27] have demonstrated that in a group of infants between the ages of 2 and 12 months the metabolism is proportional to weight rather than to surface area, and have pointed out the effect of age, showing that among infants of the same age the metabolism is proportional to the

27. Murlin and Hoobler: The Energy Requirement of Normal and Marasmic Children with Special Reference to the Specific Gravity of the Child's Body, Proc. Soc. Exper. Biol. and Med., 1914, xi, 115.

surface area. Benedict and Talbot[28] believe that the metabolism of infants is not proportional to surface area, but is proportional to protoplasmic mass. Table 7 shows that comparing babies and dogs with adults the method of surface area gives results much closer to the average for men than the method of comparison by weight. It may seem superfluous at this late date to argue at length in support of Rubner's law of surface area, but this law is becoming the center of an active discussion.

The percentage of calories derived from protein in the fasting experiments is a matter of some interest in the discussion of the subject of the toxic destruction of protein. The average figures for the basal experiments on the various subjects are as follows: G. L., 16.5 per cent.; E. F. D. B., 19 per cent.; F. C. G., 18 per cent.; Louis M., 22 per cent.; John L., 15 per cent.; L. C. M., 21.5 per cent. To this list may be added the figures for several normal controls from the work of Benedict and Joslin:[29] F. G. B., 17.6 per cent.; J. R., 15.6 per cent.; J. J. C., 15.7 per cent.; D. B., 21.6 per cent.; H. F. T., 19.9 per cent.; Dr. S., 15.5 per cent.; V. G., 12.7 per cent.; T. M. C., 14.8 per cent. These figures represent largely the effect of the amount of protein in the diet of the preceding day. They are by no means the figures that would be obtained had the subjects been maintained on a protein minimum for a few days before the experiments.

THE EFFECTS OF FOOD

The experiments on the effects of food were intended primarily as controls on the effects of similar meals given to patients with typhoid fever and exophthalmic goiter. While the subject of the specific dynamic action of food is one of great interest and importance it was felt that the chief function of the calorimeter in Bellevue Hospital was the investigation of pathological conditions. Consequently, very simple protein and carbohydrate meals which could be given in typhoid fever were the only ones studied, and the study of the effects of fat was postponed. During the season of 1913 commercial glucose containing dextrose 42.37 per cent., dextrin 44.57 per cent. and water 13.50 per cent. was used. This is one of the cheapest of food-stuffs, is readily soluble in water, is not very sweet and on account of its chemical composition should be rapidly absorbed. It has been found of great service

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28. Benedict and Talbot: Studies in Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1; Gaseous Metabolism of Infants, Carnegie Institution of Washington, 1914, Pub. 201.

29. Benedict and Joslin: A Study of Metabolism in Severe Diabetes, Carnegie Institution of Washington, 1912, Pub. 176, p. 103.

in feeding many of the patients and in some ways is preferable to the less soluble lactose. In the season of 1914 chemically pure dextrose was used in order to compare its effects with that of the mixture. The chief protein meal used in typhoid consisted chiefly of casein in the form of cottage cheese and fat-free milk with the whites of two or three eggs and some egg yolk. It did not make a very palatable mixture, but it was consumed by most of the typhoid patients without much complaint and it certainly did them no harm. While it might have been more satisfactory to give meat, it did not seem justifiable until we had more experience with its effects in fever.

TABLE 7.—Comparison of Calories per Kg. and per Square Meters of Body Surface

Investigator	Subject	Calories per Kg.	Calories per Sq. M	Per Cent. Variation from Average for Men	
				According to Calories per Kg.	According to Calories per Sp.M.
Benedict and collaborators	79 men................	1.08	34.7	....	....
Lusk	Dog 1................	1.65	31.6	+53	— 9
Lusk	Dog 2................	1.75	32.7	+62	— 6
Lusk	Dog 3................	1.45	29.8	+35	—14
Lusk and McCrudden.......	Dwarf, Wt. 21.3 kg. ...	1.21	32.3	+12	— 7
Howland	Baby 1..............	2.89	39.5	+168	+14
Howland	Baby 2..............	3.45	45.7	+220	+31
Murlin and Hoobler........	Average 6 infants.....	2.69	36.3	+150	+ 5
Benedict and Talbot........	Average 10 normal in- under 1 month	1.95	25.6	+ 81	—26
	Average 11 normal infants between 1 and 10 months	2.21	35.5	+105	+ 2

Two different methods were used in obtaining a base line to represent the metabolism without food. At first the fasting metabolism was determined in the early morning and the food given while the subject was in the calorimeter. This necessitated a sojourn of three or four hours in the box after the food in addition to the two hours before the food. Even normal individuals become tired after three hours of absolute quiet in a calorimeter and it was evident that patients would be restless in such long experiments. Another disturbing factor was the gradual change in the metabolism with the different hours of the day. The method finally adopted has given great satisfaction. It is the method used so successfully by Lusk[2] on the dog. The basal metabolism is determined in a two- or three-hour experiment and two

days later the food is given before the subject is sealed in the box and the metabolism determined during the same hours studied in the fasting experiment. The basal metabolism in our experience does not change rapidly enough to make this method inaccurate. The high metabolism in the first experiment on E. F. D. B. was due to restlessness, and the low metabolism in the first experiment on F. C. G. was due to profound sleep. Between May 17, 1913, and May 18, 1914, the heat production of E. F. D. B. did not vary 3 per cent. in the three

TABLE 8.—Increase in Heat Production Following Ingestion of Dextrose

Subject	Hours After Glucose	Per Cent. Rise	Extra Calories	Extra Calories from Combustion of Carbohydrate	Specific Dynamic Action, Per Cent.
G. L.: 100 glucose............	0-1	20	15.52	.....	..
	1-2	10	8.16	.....	..
	2-3	3	2.26	.....	..
E. F. D. B.: 100 glucose.....	0-1	3	2.63	24.56	11
	1-2	11	8.78	22.38	39
	2-3	9	6.77	20.41	39
	3-4	6	4.28	23.96	18
Total	...	..	22.46	91.31	Av. 25
E. F. D. B.: 200 glucose.....	1-2	13	9.18	41.68	22
	2-3	17	11.73	37.83	31
	3-4	8	5.98	39.22	15
	4-5	7	5.12	40.08	13
Total	...	..	32.01	158.81	Av. 20
L. C. M.: 200 glucose........	1-2	24	15.09	33.37	45
	2-3	16	10.49	41.04	26
	3-4	16	10.25	40.85	25
Total	...	..	35.83	115.26	Av. 31

tests made. In some of the ward patients studied the metabolism has remained constant from day to day and even in typhoid fever has changed in gradual curves. Two hundred grams of dextrose or its equivalent caused an average increase of 12.5 per cent. in the first three to six hours after its ingestion. One hundred grams caused an average increase of 9 per cent. The casein meal with 10.5 gm. N increased the metabolism 12 per cent., the beef with almost 24 gm. nitrogen increased

it 22 per cent.* A more detailed study of the effects of food is given in Tables 8 and 9, which show the effects in the different periods. The percentage increase in metabolism and the extra calories produced are calculated from the nearest basal determination. The extra protein calories produced are calculated from the increase in the urine nitrogen above the average hourly elimination of the nearest basal determination. The extra grams of urinary nitrogen when multiplied by the factor 26.51 give the extra calories from the combustion of protein during that hour. The extra calories produced when divided by this

TABLE 9.—Increase in Heat Production Following Protein Meal

Time After Protein Meal, Hours	Per Cent. Rise in Metabolism	Extra Calories Produced	Extra Protein Calories Metabolized. Extra Urine N × 26.51	Specific Dynamic Action, Per Cent.
E. F. D. B.: 10.5 N				
1½ to 2½	8.0	5.93	8.96	60
2½ to 3½	16.5	12.34	8.27	140
3½ to 4½	12.1	9.03	10.13	90
4½ to 5½	15.6	11.54	1.56	738
5½ to 6½	6.8	5.04	1.56	300
Total	....	43.88	30.48	Av. 144
Louis M.: After 23.93 N				
2 to 3	15.1	9.68	4.80	203
3 to 4	16.2	10.36	4.59	225
4 to 5	28.0	17.94	11.88	151
5 to 6	27.5	17.62	13.04	135
6 to 7	17.6	11.30	16.33	69
7 to 8	25.7	16.45	15.64	106
Total	....	83.35	66.28	Av. 126

figure for the extra protein calories metabolized, give the specific dynamic action in the sense of Rubner (see Note 2, Williams, Riche and Lusk, p. 370), amounting to as much as 144 per cent. and 126 per cent. for the two experiments. The accuracy of this method of calculation may be impaired by the lag in the excretion of nitrogen by

* Since the completion of this paper two more normal men have been given the test meals. Morris S. on Dec. 18, 1914, showed a rise of 6.5 per cent. after a meal containing 9.6 gm. nitrogen. Albert G. on Jan. 6, 1915, showed an increase of 9 per cent. in his metabolism after 115 gm. commercial glucose (100 gm. dry glucose).

the kidneys. In the dextrose experiments the method of calculation is slightly different from the method used by Lusk.[2] The extra calories produced by the combustion of carbohydrate are reckoned as follows: In the nearest basal determination the average figure for the calories per hour is multiplied by the percentage of calories furnished by the combustion of carbohydrate. A similar calculation is made in each hour of the experiment in which dextrose was administered and the extra carbohydrate calories metabolized in each hour determined. This figure divided into the extra calories produced gives the specific dynamic action of 25, 20 and 31 per cent. in the three experiments.

SUMMARY AND CONCLUSIONS

Seven normal men were studied with and without food as controls for the observations on patients in the metabolism ward. Their average basal metabolism (at perfect rest, fourteen to eighteen hours after their last meal) was 34.8 calories per hour per square meter of body surface. The average basal metabolism of 89 normal men studied by Benedict, Emmes, Roth and Smith[10] was 34.7 calories. The average of the 7 men studied in the Sage bed calorimeter in Bellevue and of the 5 men studied in Benedict's bed calorimeter in Boston was 34.2 calories. As a result we have adopted the figure of 34.7 calories per square meter of the body surface as the average heat production of normal men between the ages of 20 and 50 years.

All of the subjects studied in the bed calorimeter were within 11 per cent. of this average. Of the 79 men of normal figure between the ages of 20 and 50 studied by Benedict and collaborators, 86 per cent. were within 10 per cent. of the average and the remainder between 11 and 15 per cent. If, therefore, the heat production of a given subject suffering from some pathological condition is more than 10 per cent. above or below the average it may be regarded as abnormal, but cannot be proved abnormal unless the departure from the average is at least 15 per cent.

Groups of men of weights between 45 and 85 kilograms show a mean heat production within 2 per cent. of the average according to surface area. According to calories per kilogram of body weight the group weighing between 75 and 85 kg. produces 7 per cent. less than the average figure and the group between 45 and 55 kg. produces 9 per cent. more than the average. The conclusion is therefore drawn that among groups of men of varying weights metabolism is proportional to surface area according to Rubner's law and is not proportional to body weight. By using the surface area as a basis one can refer all individuals to a single average normal figure, 34.7. If one uses the body weight as a basis a different normal figure is required for each weight.

The methods of direct and indirect calorimetry in disease agree in two- and three-hour periods; and in health may be found to agree in hourly periods. In the total measurement of 4,577 calories in the experiments reported in this paper the two methods have agreed within 0.17 per cent. In a total of thirty one-hour periods on one normal subject the two methods have agreed within 5 per cent. in twenty-one individual hours and within 10 per cent. in twenty-seven of the periods.

The method of indirect calorimetry using the oxygen consumption as a basis gives the best results in hourly periods. The method of direct calorimetry in short periods is made difficult by uncertainty as to the correct specific heat of the body and also by the fact that the different parts of the body do not always change their temperatures at the same rate. On the average one obtains the best results by considering that the rectal temperature change indicates the mean temperature change of the body, but in typhoid fever the surface thermometers often give a better indication of the mean body change.

The most satisfactory method of determining the effect of food in increasing heat production in normal subjects and patients is to determine the basal metabolism at frequent intervals, and on days shortly after a basal determination administer the food before the subject is sealed in the calorimeter. It has been found that 200 gm. of dextrose or its equivalent in commercial glucose or a casein meal with 10.5 gm. of nitrogen increase the heat production by about 12 per cent. over a period of three to six hours. The basal metabolism of patients with various diseases and the effects of this same food will be discussed in subsequent publications.

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CLINICAL CALORIMETRY

FIFTH PAPER

THE MEASUREMENT OF THE SURFACE AREA OF MAN *

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Recent work on the basal metabolism of infants and adults has revived interest in Rubner's law that heat production in different individuals and species of animals is proportional to the surface area. This law was first definitely formulated by Rubner[1] in 1883, although suggested by Bergman[2] many years before. At the time the experimental work in support of this theory was done no record was kept of body movements and men and animals were allowed to move during the periods of investigation. The average heat production per square meter of body surface was about 1,000 calories per day. In modern work, where the influence of muscular activity is absolutely excluded, the figure is in the neighborhood of 830 calories per square meter per day, as has been shown in Paper 4 of this series. With these new figures it is not unnatural that many investigators have felt that the whole question must be studied anew. Very recently Murlin and Hoobler[3] in New York and Benedict and Talbot[4] in Boston have all concluded that among infants metabolism is more nearly proportional to body weight than to surface area. If this is true for adults, it is a matter of great theoretical and practical importance.

It is obvious that the whole question rests on the accuracy of the determinations of the basal metabolism and of the surface area. The methods of determining the metabolism have been greatly improved, leaving the surface area the doubtful factor. The number of formulas for surface area determination is large, the number of individuals

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* From the Russell Sage Institute of Pathology, in affiliation with the Second Medical Division of Bellevue Hospital.

1. Rubner: Ueber den Einfluss der Körpergrosse auf Stoff- und Kraftwechsel, Ztschr. f. Biol., 1883, xix, 545.

2. Bergman: Wärmeökonomie der Thiere, Göttingen, 1848, p. 9.

3. Murlin and Hoobler: The Energy Metabolism of Normal and Marasmic Children with Special Reference to the Specific Gravity of the Child's Body, Proc. Soc. Exper. Biol. and Med., 1914, xi, 115.

4. Benedict and Talbot: Studies in the Respiratory Exchange of Infants, Am. Jour. Dis. Child., 1914, viii, 1; The Gaseous Metabolism of Infants, Carnegie Institution of Washington, 1914, Pub. 201.

whose area has been measured is small. In 1879 Meeh[5] finished his painstaking and time-consuming work which has remained the standard ever since. He measured six adults and ten children, using a variety of methods. Some parts of the body were marked out in geometrical patterns, which were then traced on transparent paper. The areas of these were then determined by geometry, or, if the pieces of paper were very irregular, by weighing. Some of the cylindrical parts of the body were wound with strips of millimeter paper like a bandage. Funke[6] in one case covered the skin of a cadaver with adhesive material and pasted over this squares of paper. Fubini and Ronchi[7] measured one man by marking out the anatomical regions of the body and determining the areas geometrically. Bouchard[8] used this same method in measuring a number of adults. He speaks of a plan of clothing the body in tights made of some thin, flexible, inelastic sort of paper, the area of which could be determined by weighing. Apparently, he was not able to find the right material. He mentions the fact that M. Bergonie measured surface area by means of plates of lead, and that M. Roussy used a very ingenious cylinder with a revolution counter which he passed over the whole surface of the body. Bouchard also states that D'Arsonval determined the surface area electrically by clothing the man in silk tights and charging him as one would charge a Leyden jar, calculating the surface by applying a metal plate of known area. Lissauer[9] measured twelve dead babies by covering the skin with colored adhesive material and then applying silk paper and measuring the area of the paper geometrically or with a planimeter.

Meeh[5] as a result of his own measurements, based his formula for determining surface area on the fundamental mathematical law that the surfaces of similar solids are proportional to the ⅔ power of their volumes. Using the body weight to represent volume he determined that the constant 12.312 when multiplied by the cube root of the square of the weight in kilograms gave results which came within 7 per cent. of all his measurements of adults and older children. The constant for infants was 11.9 and for various species of animals still different. Miwa and Stöltzner[10] felt the need of introducing linear measurements

5. Meeh: Oberflächenmessungen des menschlichen Körpers, Ztschr. f. Biol., 1879, xv, 425.

6. Funke: Moleschott's Untersuchungen, z. Naturlehre, 1858, iv, 36.

7. Fubini and Ronchi: Ueber die Perspiration der CO_2 beim Menschen Moleschott's Untersuchungen, z. Naturlehre, 1881, xii.

8. Bouchard, Ch.: Traité de Pathologie générale, Paris, 1900, iii[1], 200, 384.

9. Lissauer, W.: Ueber Oberflächenmessungen an Säuglingen und ihre Bedeutung für den Nahrungsbedarf, Jahrb. f. Kinderh., 1902, lviii, 392.

10. Miwa and Stöltzner: Bestimmung der Körperoberfläche des Menschen. Ztschr. f. Biol., 1898, xxxvi, 314.

and chose the height (L) and the circumference of the chest (U) at the level of the nipples in men and just above the breasts in women, retaining the weight (G) as a factor. Using Meeh's measurements they determined by means of the following formula,

$$\text{Surface} = \frac{K\ UGL}{\sqrt[6]{G^4L^4U^2}} \text{ using an average constant (K) of 4.5335.}$$

This formula, which might have been simplified to $\text{Surface} = K\sqrt[3]{U^2GL}$ has never been much used, although its originators have shown that it comes closer to Meeh's cases than Meeh's own formula. Lissauer from the measurement of babies, almost all of whom were atrophic, retained the principles of Meeh's formula, but found that the constant 10.3 gave better results than the constant 11.9. This indicated that Meeh's figure was about 16 per cent. too high. The formula of Miwa and Stöltzner, according to Lissauer, gave no better results than that of Meeh. Howland and Dana,[11] using the measurements of Meeh and Lissauer, have devised a simple formula in which the surface area (y) of the child equals the weight in grams (x) multiplied by a constant 0.483 (m) plus 730 (b). This is expressed in the terms $y = mx + b$.

Bouchard found a consistent plus error in Meeh's formula as given in Table 1. In his own formula, which requires twenty-five pages of tables for its application, he uses the body weight, the height and the diagonal circumference of the abdomen from the hollow of the back to a point somewhere above the umbilicus according to the degree of obesity. Bouchard states that a measuring tape passed around the abdomen and moved back and forth will of itself find the right circumference, which he calls the "tour de taille." Bouchard's formula has been very little used, as it seems to be difficult to understand and apply.

Recently Dreyer, Ray and Walker[12] have made many measurements of birds and small mammals and have found that the surface area, blood volume, cross sections of the aorta and trachea are all nearly proportional to the ⅔ power of the weight. The formula which applies to all these measurements is $S = k\,W^n$, in which S is the surface, blood volume, etc.; k is a constant which varies with the species; W is the weight, and n is approximately 0.70-0.72 instead of 0.666 which would be the ⅔ power. Benedict and Talbot[4] have suggested that the active mass of protoplasmic tissue develops normally on this ratio. They are convinced that metabolism is determined, not by the body

11. Howland and Dana: A Formula for the Determination of the Surface Area of Infants, Am. Jour. Dis. Child., 1913, vi, 33.

12. Dreyer and Ray: Phil. Trans., 1909-10, cci, Series B, p. 133. Dreyer, Ray and Walker: The Size of the Aorta in Warm-Blooded Animals and its Relationship to Body Weight and to Surface Area, Expressed in a Formula, Proc. Roy. Soc., 1912-1913, lxxxvi, Series B, pp. 39 and 56.

surface, but by the active mass of protoplasmic tissue. If both are assumed proportional to the same thing, it will be a difficult matter to prove which is the more important factor.

As shown in Paper 4 of this series, the metabolism of the normal and pathological subjects studied in the Sage respiration calorimeter in Bellevue Hospital has been expressed in terms of calories per square meter per hour. The work had progressed but a short distance when it was obvious that no formula based on weight could give the surface area of all the patients with any great degree of accuracy. Among the patients studied were men emaciated from typhoid fever and hyperthyroidism, men of normal shape and men with acromegaluy, hypophysial dystrophy and cretinism. Eventually, it is hoped every conceivable shape will be studied. A formula such as Meeh's is accurate only for objects of different size, *but of similar shape.*

TABLE 1.—Determination of Error in Meeh's Formula as Applied to Measured Individuals

Subject	Observer	Weight, Kg.	Surface Area as Measured, Sq. Cm.	Constant for Meeh's Formula, Area Divided by Wt.⅔	Error in Meeh's Formula	Age, Yrs.	Height, Cm.	Body Form
Benny L.	D.B. and D.B.	24.2	8,473	10.13	+21	36	110.3	Cretin. Short and fat.
Hagenlocher	Meeh................	28.30	11,883	12.80	— 4	13.1	137.5	Medium strong.
Very thin woman	Bouchard...........	31.8	12,737	12.69	— 3	...	....	Very thin.
Korner	Meeh................	35.38	14,988	13.17	— 7	15.7	152	Muscular.
Schneck	Meeh................	50.00	17,415	12.96	— 5	36	158	Very thin.
Adult man	Fobini and Ronchi	50.00	16,067	11.84	+ 4	...	....	?
Nagel	Meeh................	51.75	18,158	12.96	— 5	45	160	Somewhat thin.
Fr. Brotbeck ...	Meeh................	55.75	19,206	13.16	— 6	17.7	169	Very strong and muscular.
Naser	Meeh................	59.50	18,695	12.27	+ 0	...	170	Somewhat thin, but well proportioned.
Normal man	Bouchard...........	61.6	18,930	12.13	+ 2	...	....	Normal man.
Fr. Haug	Meeh................	62.25	19,204	12.01	+ 2	26.2	162	Strong.
Morris S.	D.B. and D.B.	64.0	16,720	10.45	+17	21	164.3	Short and rather stout.
R. H. H.	D.B. and D.B.	64.08	18,375	11.49	+ 7	22	178	Tall and thin.
Forsthauer	Meeh................	65.50	20,172	12.48	— 1	66	172	Still very strong.
E. F. D. B.	D.B. and D.B.	74.05	19,000	10.55	+14	32	179.2	Tall, average build.
Normal woman..	Bouchard...........	76.5	19,484	10.81	+14	...	....	Normal woman.
Kehrer	Meeh................	78.25	22,435	12.26	+ 0	36	171	Corpulent.
Large man	Bouchard...........	88.6	21,925	11.03	+12	...	....	Large strong man.
Mrs. McK.	D.B. and D.B.	93.0	18,592	9.06	+36	...	149.7	Very short and very fat.
Very fat man...	Bouchard...........	140.0	24,966	9.26	+33	...	....	Very fat man.

The obvious method for determining surface area is to multiply the length by the average width. An attempt has been made to measure a characteristic length and an average or characteristic circumference of each part of the body and determine the area of the part by multiplying the two and correcting by a constant factor. The sum of the parts will then give the total surface area of the body. When the proper measurements have been selected and the constants for each part determined, it is evident that the method can be applied to individuals of varying shape no matter what disproportion may exist between the different parts of the body.

Fig. 16.—The cretin, Benny L., with mold of his surface area.

INDIVIDUALS MEASURED

The five individuals whose surface area was measured differed from each other in bodily form to a marked degree. All of them had served as the subjects of observations in which the basal metabolism was determined. Benny L. was a cretin 36 years old with the general mental and physical development of a boy of 8. As his photograph (Fig. 16) shows, he was short and stocky, with prominent abdomen, short thick extremities and rather small head. Morris S., 21 years old, was measured three months after he was discharged from the hospital, where he

had been confined three and one-half months with a severe attack of typhoid fever. He had recovered even more than his usual weight in the hospital and during the subsequent stay in the country. At the time he was measured he was of well rounded figure, almost stout. He was short and of small frame, with small hands and feet. R. H. H., a chemist, 22 years old, was tall and thin, with long, slim bones, sinewy muscles and very little subcutaneous fat. E. F. D. B., 32 years old, was tall, but of average build. Mrs. McK. was a very short and very fat woman whose metabolism had been studied in great detail by Dr. David

TABLE 2.—MEASUREMENTS USED IN FORMULA

Index Letter of Part Measured	Benny L.	Morris S.	R. H. H.	E. F. D. B.	Mrs. McK.
A	57.5	63.9	65.0	67.0	58.0
B	50.2	54.1	56.6	57.8	56.6
F	37.2	56.7	65.0	67.3	55.0
G	20.2	29.5	27.5	32.5	33.0
H	18.7	24.6	26.0	27.5	27.0
I	12.8	16.7	16.3	16.2	16.5
J	13.6	20.0	21.5	20.2	17.0
K	15.2	20.4	20.5	20.5	17.5
L	36.6	55.0	55.0	51.5	56.0
M	62.0	76.2	72.5	77.0	111.0
N	63.5	87.2	85.8	96.0	100.0
O	26.4	41.7	47.0	46.3	40.0
P	35.5	55.5	54.0	59.0	60.0
Q	61.0	96.0	93.2	96.5	117.0
R	29.3	41.7	47.0	49.4	36.8
S	23.7	35.7	33.8	37.0	41.0
T	17.7	24.8	26.2	28.3	21.5
U	16.8	22.5	22.2	23.5	19.3
V	15.7	21.2	21.2	23.5	22.0

Edsall and Dr. James H. Means in Boston. We are greatly indebted to Dr. Means for taking the measurements of this subject and for taking the mold of the surface and sending it to us to be measured.

MEASUREMENTS OF THE BODY

The individual to be measured was undressed, weighed and placed on a flat table with a vertical foot-board about 30 cm. high. All the measurements were made with the subject flat on his back with his feet against the foot-board. A steel tape was used for all the linear meas-

urements and a cloth tape for the circumferences. The measurements actually used are given in Table 2; those not used are given in Table 3 in case other investigators wish to apply different formulas.

THE MOLD OF THE BODY

The method of determining the surface area finally adopted consisted in making a thin mold of the body, cutting this up in pieces which would lie flat, printing the patterns of these pieces on photographic paper (Fig. 17) and finding the area of the printed patterns by cutting them out and weighing them. The subject was dressed in a tight-fitting suit of thin union underwear, which covered the body, arms and legs. Socks were put on the feet, thin cotton gloves on the hands, while over the head and neck was slipped a section of the leg of a knitted undersuit held in place by means of bandages. On this groundwork strips of paper were pasted until a flexible inelastic mold of the

TABLE 3.—MEASUREMENTS NOT USED IN FORMULA

Index Number of Part Measured	Benny L.	Morris S.	R. H. H.	E. F. D. B.	Mrs. McK.
I...........	24.2 kg.	64.0 kg.	64.08	74.49	93.0
II...........	110.5 cm.	164.3 cm.	178.0	179.2	149.7
III...........	88.3	135.5	148.0	147.2	125.0
IV...........	81.1	124.6	136.6	135.5	.....
V...........	83.6	124.4	139.0	141.2	125.4
VI...........	76.5	115.2	130.0	125.5	107.0
VII...........	55.7	83.4	94.0	95.7	76.8
VIII...........	46.2	72.3	84.5	85.5	60.2
IX...........	65.1	83.5	80.7	84.5	92.0
X...........	40.0	60.2	81.5	67.5	65.5
XI...........	29.6	43.6	48.0	49.0	40.0
XII...........	8.2	11.3	.....	11.7	15.8
XIII...........	17.0	24.5	27.0	28.0	21.0
XIV...........	21.2	33.1	38.5	38.5	32.0
XV...........	18.6	27.5	25.3	30.0	30.5
XVI...........	17.8	26.0	25.0	29.0	30.0
XVII...........	35.5	50.3	48.0	56.5	56.0
XVIII...........	23.2	34.7	32.7	37.5	39.0
XIX...........	22.6	31.0	31.5	33.5	30.6
XX...........	43.2	52.0	48.0	62.5	35.5
XXI...........	28.5	38.0	36.0	37.0	34.2
XXII...........	74.5	108.0	99.0	107.0	106.0

body was completed. The material used was strong manila paper, about 1½ inches broad, gummed on one side. It is manufactured in large rolls and is used by stores as a substitute for string in doing up small packages and also by some tailors in making models of their customers. For our purposes it was wound in small rolls and placed in a small brass holder which moistened the gummed side as it was applied to the cloth covering the body. It could be applied so quickly that very little

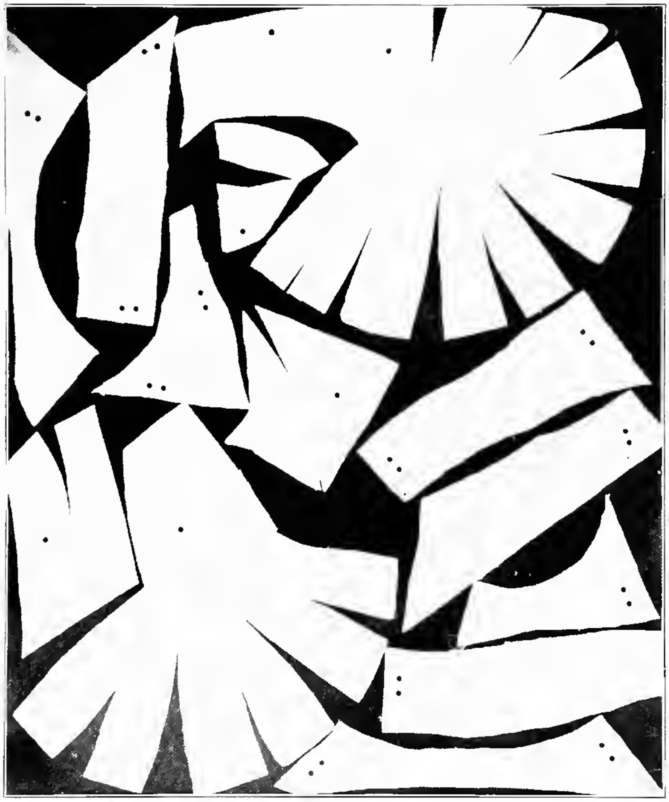

Fig. 17.—Reduced photograph of the patterns printed from the mold of the head and neck of one of the subjects measured. The patterns of the head marked with one punch were cut out and weighed separately from the pieces of the neck marked with two punches. The dark areas were also weighed as control.

time was required to cover the body. The head presented no difficulty until the nose was reached. This region was the last to which the paper was applied and a couple of holes were left for the person to breathe through. The mold of the face was then quickly opened by means of curved bandage scissors. In most cases only one arm and one leg were measured.

TABLE 4.—COMPARISON OF AREAS OF PARTS OF BODY AS ACTUALLY MEASURED AND AS CALCULATED FROM FORMULAS

Part of Body	Benny L.			Morris S.			R. H. H.			E. F. D. B.			Mrs. McK.		
	Area as Measured, Sq. Cm.	Area as Calculated from Formula, Sq. Cm.	Error in Formula, Per Cent.	Area as Measured, Sq. Cm.	Area ac Calculated from Formula, Sq. Cm.	Error in Formula, Per Cent.	Area as Measured, Sq. Cm.	Area as Calculated from Formula, Sq. Cm.	Error in Formula, Per Cent.	Area as Measured, Sq. Cm.	Area as Calculated from Formula, Sq. Cm.	Error in Formula, Per Cent.	Area as Measured, Sq. Cm.	Area as Calculated from Formula, Sq. Cm.	Error in Formula, Per Cent.
Head.......	900	888	— 1	1,030	1,064	+3	1,173	1,132	—4	1,154	1,192	+4	1,090	1,010	— 7
Arms.......	1,092	1,074	— 2	2,314	2,236	—3	2,524	2,535	+0	2,776	2,865	+3	2,298	2,351	+ 2
Hands.....	596	458	—23*	900	905	+1	968	977	+1	876	918	+5	678	660	— 3
Trunk.....	3,060	3,229	+ 6	6,304	6,318	+0	6,444	6,121	—5	6,572	6,264	—5	7,746	8,308	+ 7
Thighs......	1,284	1,294	+ 1	3,022	3,207	+6	3,712	3,512	—5	3,820	3,655	—4	3,500	3,594	+ 3
Legs........	930	973	+ 5	2,000	2,085	+4	2,396	2,225	—7	2,472	2,560	+4	2,156	2,113	— 2
Feet........	611	596	— 3	1,150	1,123	—3	1,158	1,178	+2	1,330	1,378	+4	1,124	920	—18
Total.......	8,473	8,512	+ 0.5	16,720	16,938	+1.3	18,375	17,680	—3.8	19,000	18,832	+0.9	18,592	18,956	+ 2.0

* Benny L. had chronic ulcers on his hands, and the measurement was made with difficulty. The hands of six other individuals were measured and calculated by the formula. The percentage of errors of the calculations in these cases were: —4.0, —1.8, +2.5, —1.8, +2.0 and —2.7.

The hands could not be covered satisfactorily with paper, and hard paraffin was used instead. This was melted and applied to the glove with a brush, soaking well into the meshes of the cotton. The melted paraffin was not too warm for the hands, but was uncomfortable for parts of the body which were not so accustomed to heat. Starch was tried in some instances, but dried too slowly; plaster-of-Paris was too stiff.

Certain portions of the skin were not measured by this mold. The area back of the ears was determined by tracing the back of the ears on a piece of cardboard and correcting by careful measurements. The skin between the toes was measured by tracing. The penis and scrotum were measured and the area determined geometrically. This left unmeasured only very small portions of the face and ears since the mold did not fit closely into the eye-sockets and the concavities of the ear. This error could not have amounted to more than 10 to 20 square centimeters in a total of fifteen thousand.

While the mold was still on the subject the landmarks of the body were located through the paper and the different anatomical regions marked off by drawing the borders on the paper. The mold was then removed with bandage scissors or small probe pointed scissors and the inside of the cloth covered with a thin layer of melted paraffin which, when it hardened, left a material much easier to work with than the cloth and paper alone, since this would not lie flat. Next the mold was cut at the borders of the various regions of the body and each of these regions cut into pieces which would lie flat. These pieces were then marked with a punch for identification and transferred to a large photographic printing frame. After printing in the sun and without developing or fixing, patterns of the pieces of the mold were cut out and weighed to the tenth of a milligram and the blank parts of the sheet weighed as a control. Before this printing each sheet of photographic paper was carefully measured and weighed and the area of each gram of paper determined. By weighing the patterns of each region together it was a simple matter to find the area of that region. A copy of the print made from the mold of the head and neck of one of the subjects is given in Figure 17 showing the method of cutting the paraffined mold so that it would lie flat.

ACCURACY OF METHOD

The accuracy of the procedure was tested in several ways. The bottom of a porcelain evaporating dish was measured twice with a difference of 0.1 per cent. between the two measurements. The surface of the hand of D.D.B. was measured three times, the glove being covered once with starch and on the two other occasions with paraffin.

The square centimeters of surface area as determined on the three occasions were 555.5, 556.0 and 555.5. The right and left sides of the whole body of Benny L. measured separately, agreed within 0.5 per cent.

MEASUREMENTS

The body was divided into the larger regions used by Meeh. An effort was made to select the measurements which represented the length and average breadth of the part. The head region included the ears and the trunk included the neck, the breasts in the female, and the penis and scrotum in the male.

DETERMINATION OF NEW FORMULA

Having measured the surface areas of the different parts of the body and the linear measurements of these parts, the formula to determine the surface area of each part was calculated as follows: the various measurements of length were multiplied by various sums of the measurements representing the width; the resulting figure was divided by the surface area as actually measured. The factors resulting from this calculation in each of the five individuals were compared to determine the percentage variation. That particular combination of length and breadth measurements which showed the smallest variation was chosen and the reciprocal of the average factor for this combination taken as a constant. Fortunately the best results were always obtained by using measurements which were simple. The factors include the multiplication by two necessary to give the area of the right and left arm, hand, etc.

MEASUREMENTS USED IN FORMULA (TABLE 2).

HEAD: AB 0.308.
- A—Around vertex and chin.
- B—Around occiput and forehead, just above eyebrows.

ARMS: F(G + H + 1) 0.558.
- F—Outer end of clavicle to lower border of radius.
- G—Circumference at level of upper border of axilla.
- H—Largest circumference of forearm.
- I—Smallest circumference of wrist.

HANDS: JK 2.22.
- J—Lower posterior border of radius to tip of second finger.
- K—Circumference of open hand.

TRUNK: L(M + N) 0.703.
- L—Suprasternal notch to upper border of pubes.
- M—Circumference of abdomen at level of umbilicus.
- N—Circumference of thorax at level of nipples in the male, and just above breasts in the female.

THIGHS: O(P + Q) 0.508.
- O—Superior border of the great trochanter to the lower border of the patella.
- P—Circumference of thigh just below the level of the perineum.
- Q—Circumference of hips and buttocks at level of trochanters.

LEGS: RS 1.40.

R—From sole of foot to lower border of patella.

S—Circumference at level of lower border of patella.

FEET: T(U + V) 1.04.

T—Length of Foot.

U—Circumference of foot at base of little toe.

V—Smallest circumference of ankle.

MEASUREMENTS NOT USED IN FORMULA (TABLE 3)

I—Weight.

II—Height.

III—Sole of foot to suprasternal notch.

IV—Sole of foot to level of nipples.

V—Sole of foot to upper border of axilla.

VI—Sole of foot to tip of ensiform process.

VII—Sole of foot to superior border of great trochanter.

VIII—Sole of foot to perineum.

IX—Circumference of body at level of tip of ensiform.

X—Tip of second finger to upper border of axilla.

XI—Tip of second finger to tip of olecranon process.

XII—Tip of second finger to metacarpo-phalangeal joint.

XIII—Tip of olecranon to lower border of radius.

XIV—Tip of olecranon to outer end of clavicle.

XV—Circumference of arm at the insertion of the deltoid.

XVI—Circumference of arm at belly of biceps.

XVII—Circumference of thigh half way between anterior superior spine of the ilium and the lower border of the patella.

XVIII—Largest circumference of calf.

XIX—Circumference of foot around heel.

XX—From back of neck around superior maxilla just below ears and nose.

XXI—Around neck just below larynx.

XXII—Around shoulders at level of heads of humeri.

BORDERS OF REGIONS OF BODY:

Head: Lower margin of the mandible to its posterior border, thence to tip of the mastoid process and in a straight line to the external occipital protuberance.

Arm: From the acromion process anteriorly and posteriorly to the upper border of the axilla.

Hand: Line at right angles to long axis of forearm drawn at level of tip of ulna.

Thigh: From the perineal point going posteriorly in the natal fold to the upper border of the great trochanter, thence medially in a straight line to the perineal point.

Leg: Line at level of lower border of patella.

Foot: Line at level of tip of lateral malleolus.

DISCUSSION OF RESULTS

Table 1 shows that the constant employed by Meeh has not been confirmed by subsequent observers. It gives results which are too high in every case except one very thin woman. Lissauer found Meeh's figure for infants 16 per cent. too high. Bouchard in four of his five cases found it from 2 to 33 per cent. too high, while in our five cases we have found it from 7 to 36 per cent. too high. The majority of Meeh's

subjects seem to have been thin, and the error of the formula is very great in fat individuals. One can perhaps obtain fairly accurate results in using Meeh's formula if one retains the factor of 12.3 for thin subjects, 11 to 12 for people of average build, 10 to 11 for the moderately stout and 9 to 10 for the very fat. Possibly at some later date a more accurate factor can be determined by the relationship of weight to height, retaining Meeh's fundamental principle of the ⅔ power of the weight.

Miwa and Stöltzner's formula gives results only slightly better than Meeh's. The errors in calculated areas of our five subjects using their formula are as follows: Benny L. + 18 per cent., Morris S. + 17 per cent., R. H. H. + 8 per cent., E. F. D.B. + 18.5 per cent., Mrs. McK. + 26.5 per cent. If the constant of 3.84 were used instead of 4.5335 the results would be much better for this series.

The series of five individuals measured by us is perhaps too small to determine factors which will remain unaltered by subsequent research, but it is doubtful if the changes will be of significance. The range of body shape among our subjects was, however, very great, and the error of the factors comparatively small. The principle of the method has been demonstrated to be sound. Unfortunately, it involves the taking of nineteen measurements, a matter of perhaps fifteen minutes time. Subsequent investigation may reduce the number, but it is difficult to see how one can avoid measuring each part of the body if one wishes to obtain accurate results on people whose shapes do not correspond closely to the average.

In any discussion as to whether metabolism is proportional to body weight or to surface area it is essential to apply a method of measuring the surface which does not depend entirely on weight. The key to the question may perhaps be found in those individuals whose surface area is not proportional to the ⅔ power of their weight, multiplied by a constant determined by measurements of average individuals.

SUMMARY AND CONCLUSIONS

The discussion of the relationship of metabolism to surface area has been based almost entirely on Meeh's formula as determined in 1879. Subsequent observers have found a consistent plus error in this formula amounting to as much as 36 per cent. in the case of very fat individuals.

The surface area of the various parts of the body can be determined as follows: A mold of the surface is made by pasting paper over tight-fitting underwear. The area of the mold is then determined by cutting it in pieces, printing a pattern on photographic paper, cutting out the pieces of the pattern and weighing them.

To determine the area of each part of the body by linear measurements alone a formula has been devised on the principle of length times the average breadth times a constant. The sum of these parts gives the total surface area of the body.

Five individuals of widely varying shapes have been measured and the surface area as calculated from the formulas compared with the surface area as actually measured. In the five cases the average error was 1.7 per cent.

In discussing the question as to whether the basal metabolism is proportional to surface area or to weight it is preferable to determine the surface area by a formula which is not of necessity a function of the weight.

Note.—Since this article was submitted for publication the formula has been tested on a tall and exceedingly thin boy, 18 years old. This patient, Gerald S., came to the hospital much emaciated from diabetes and was kept for eleven days practically without food, receiving only whisky. The mold of the body was taken on Dec. 1, 1914, shortly after his fast. At this time he weighed 45.25 kg. His surface area according to Meeh's formula was 1.563 square meters. The mold was kindly measured for us by Miss Margaret Sawyer who obtained the following figures:

	Actual Area as Measured sq. cm.	Area as Calculated from Formula sq. cm.	Error in Formula Per Cent.
Head	950	978	+ 3
Arms	2,052	2,047	— 0
Hands	847	875	— 0
Thighs	3,002	2,677	—11
Trunk	5,003	4,158	—17
Legs	1,876	2,144	+14
Feet	1,042	1,055	+ 1
Totals	14,801	13,934	— 5.8

CLINICAL CALORIMETRY

SIXTH PAPER

NOTES ON THE ABSORPTION OF FAT AND PROTEIN IN TYPHOID FEVER*

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In the course of other work on metabolism in typhoid fever it became advisable to analyze the feces of the patients. While these analyses constitute only a part of the problem in hand, the paucity of studies on the absorption of food in the febrile state appears to warrant publication of the results as a separate communication. For a complete discussion of the absorption of food in typhoid fever the reader is referred to the paper of Du Bois.[1]

Seven cases in all have been studied. The diets administered were modifications of the high calory diet employed in this clinic, that is, the proportions of fat and carbohydrate were varied to satisfy the requirements of the problem under investigation.

METHODS OF CHEMICAL ANALYSIS

Urine and feces were collected in the manner described by Gephart and Du Bois.[2] The analysis consisted in the determination of fat and nitrogen in the feces and total nitrogen in the urine. Nitrogen was determined in all cases by the well known Kjeldahl method, fat in the feces was determined in part by the Kumagawa-Suto method, and later by a saponification procedure described by one of us.[3] Carbohydrate in the feces was not determined (see work of DuBois).

CLINICAL DATA

All of the patients were admitted to Bellevue Hospital during 1913. As is customary on the service, each patient was given an enema every morning. Except when otherwise stated, the patients had from one to two formed or semiformed stools a day.

Emil C., aged 22 years, was admitted August 23, the fifth day of the disease. Widal reaction and blood culture positive. Illness, severe. The original fever lasted twenty-three days. After two days of normal temperature, the patient developed a severe relapse of twenty days' duration.

Thomas B., aged 60 years, admitted October 2, the fifteenth day of the disease. Widal reaction and blood culture positive. Illness, mild. Duration

* From the Russell Sage Institute of Pathology, in Affiliation with the Second Medical Division of Bellevue Hospital.

1. DuBois, E. F.: The Archives Int. Med., 1912, x, 177.

2. Gephart, F. C., and DuBois, E. F.: The Organization of a Small Metabolism Ward, p. 829.

3. Gephart and Csonka: On the Estimation of Fat in Feces, Jour. Biol. Chem., 1914, xix, 521.

TABLE 1.—DAILY AVERAGES OF PERIODS

Patient and Weight	No. of Period	Stage of Typhoid Fever	Dates and Days of Disease, Inclusive	Range of Maximum Temp. F.	Food During Period, Averages per Day			Analysis of Feces, Average per Day		Percentage Loss in Feces	
					Carb., Gm.	Fat, Gm.	Nitrogen, Gm.	Fat, Gm.	Nitrogen, Gm.	Fat	Nitrogen
Emil C. ...... 60-62 Kg.	1	Early and late steep curve.	Sept. 11-16 (25-30)	100.6-102.6	162	210	14.9	6.07	1.19	2.9	8.0
	2	Late steep curve..........	Sept. 17-21 (31-35)	99.8-101.0	483	74	15.0	6.30	2.89	8.5	19.3
		Relapse									
	3	Ascend. Temp. and early steep curve.	Sept. 22-Oct. 3 (36-47)	100.0-104.8	331	127	13.6	2.53	1.24	2.0	9.1
	4	Early and late steep curve.	Oct. 4-7 (48-50)	102.0-104.0	174	225	15.0	7.85	2.31	3.6	15.4
Thomas B. .. 74-76 Kg.	1	Contin. Temp.	Oct. 7-10 (20-23)	103.0-104.0	164	211	15.0	9.19	2.09	4.4	13.9
	2	Early steep curve........	Oct. 11-13 (24-26)	102.4-103.0	479	71	14.9	5.80	1.89	8.2	12.6
	3	Late steep curve..........	Oct. 14-15 (27-29)	101.0-103.0	157	204	13.8	5.02	1.28	2.5	9.3
Christian M. 80-82 Kg.	1	Late steep curve..........	Sept. 17-21 (24-28)	100.8-101.8	483	74	15.0	7.04	2.38	9.5	15.9
	2	First week conval.	Sept. 22-25 (29-32)	99.0- 99.6	160	210	15.1	6.85	1.62	3.3	10.7
	3	First week conval.	Sept. 26-28 (33-35)	99.0- 99.4	431	165	16.6	7.60	1.97	4.6	11.9
Ernest H. ... 91-92 Kg.	1	Early steep curve.........	Sept. 20-23 (18-21)	101.2-103.0	160	212	15.4	7.08	1.83	3.3	11.9
	2	Late steep curve..........	Sept. 24-27 (22-25)	100.4-101.6	479	71	15.0	3.75	1.67	5.3	11.1
	3	First week conval.	Sept. 28-Oct. 1 (26-29)	99.8-100.0	226	286	15.3	6.53	1.47	2.3	9.6
Anton K. .... 50-62 Kg.	1	Contin. temp. and early steep curve.	Oct. 7-10 (16-19)	103.8-104.6	47	273	15.0	6.61	1.37	2.4	9.1
	2	Early and late steep curve	Oct. 11-16 (20-25)	99.8-103.8	386	56	12.0	3.93	1.24	7.0	10.3
Richard T. .. 36 Kg.	1	Early steep curve.........	Oct. 17-25 (18-26)	101.0-104.2	285	57	14.3	1.63	0.84	2.9	5.8
Morris S. .... 49.8 Kg.	1	Early steep curve.........	Oct. 30-Nov. 5 (20-26)	102.2-104.0	309	143	15.6	9.74	2.60	6.8	14.8

of original fever, thirty-one days. After fourteen days of normal temperature the patient developed a relapse which lasted twenty days. The relapse was complicated by acute fibrinous pleurisy.

Christian M., aged 31 years, admitted September 8, the fifteenth day of the disease. Widal reaction and blood culture positive. Illness, mild. Duration of fever thirty days.

Ernest H., aged 30 years, admitted September 16, the fourteenth day of the disease. Blood culture and Widal reaction negative, though clinically the disease was undoubtedly typhoid fever. The illness was mild, the fever lasting twenty-four days.

Anton K., aged 18 years, admitted September 30, the ninth day of the disease. Blood culture positive. Illness, severe. Duration of fever twenty-five days. The patient suffered from diarrhea from the eleventh to the sixteenth day, passing three to nine stools a day. The first period of the analyses was not begun until the diarrhea had ceased.

Richard T., aged 14 years, admitted October 6, the seventh day of the disease. Widal and blood culture positive. Illness, severe. Duration of fever twenty-eight days. Mild cholecystitis developed on the twenty-fifth day. After one day of normal temperature a relapse occurred which lasted one week.

Morris S., aged 21 years, admitted October 17, the seventh day of the disease. Blood culture positive. Illness severe. Duration of fever thirty-four days. The patient suffered two relapses, the first severe, beginning on the thirty-sixth day and lasting twenty days; the second mild, beginning on the sixty-eighth day and continuing nine days.

TABLE 2.—Daily Averages and Percentage Loss

Stage of Disease	No. of Periods	Av. Food Fat Gm.	Average Daily Loss		Percentage Loss	
			Fat, Gm.	Nitrogen, Gm.	Fat	Nitrogen
Cont'd temperature	3	204	6.11	1.20	2.9	10.7
Low fat, steep curve..........	6	67	4.74	1.82	6.9	12.5
High fat, steep curve.......	5	199	7.15	1.84	3.8	11.9
Convalescence	3	220	6.99	1.69	3.4	10.7
Totals	17	...	6.25	1.57	4.3	11.2

DISCUSSION OF RESULTS

In Table 1 the results are expressed in terms of daily averages for the periods, which lasted from three to twelve days. The stage of the disease is designated by a description of the character of the temperature curve rather than by the actual day of the illness. As in previous papers, the stage of ascending temperature corresponds to the "first week," that of continued temperature to the "second week," that of the early steep-curve to the "third week," and that of the late steep-curve to the "fourth week." In the last two columns the losses are expressed in terms of percentage.

A summary of all the periods, in daily averages according to the stage of the disease, is given in Table 2.

ABSORPTION OF FAT

The total fat in the stools varied from 1.63 to 9.74 gm.

The mere statement of the amounts, however, conveys but little information; the stage of the disease and the quantity of fat in the food must be taken into consideration for a complete interpretation of the results. Likewise it should be stated that the expression of the results in percentage values is apt to be misleading unless one bears in mind that even the stools of fasting persons contain fat.

In the ascending and continuous temperature stages when the fat in the food varied from 127 to 273 gm. the total fat lost was from 2.53 to 9.19 gm. The percentage loss varied from 2.0 per cent. to 4.4 per cent.

The average total loss for this stage of the disease was 6.11 gm.; the average percentage loss was 2.9 per cent.

The results in the early and late steep-curve stages fall into two groups, according to the amount of fat which the patient received in his food.

Patients receiving from 56 to 74 gm. lost in the stools from 1.63 to 7.04 gm. of total fat, with an average loss of 4.4 gm. Attention should be directed to the unusually small loss of 1.63 gm. when the patient received 57 gm. The average percentage loss for this group was 6.9 per cent.

With patients receiving from 143 to 225 gm. of fat in the food, the total loss varied from 5.02 to 9.74 gm., with an average loss of 7.15 gm. In this group the relatively large loss of 9.74 gm. when the patient took only 143 gm. in the food should be noted. The average percentage loss for the group was 3.8 per cent.

In convalescence the total fat intake varied from 165 to 286 gm. The fat loss varied from 6.53 to 7.60 gm. The percentage loss was from 2.3 per cent. to 4.6 per cent.

If only those periods be considered in which the fat intake was relatively large, the percentage fat loss in the stools for all stages of the disease was 3.5 per cent. The loss in the febrile stage was 3.3 per cent., in convalescence it was 3.4 per cent. In other words, the patients in this series absorbed fat as well in the febrile stage of the disease as in convalescence.

The average fat loss for all the patients in all stages of the disease amounted to 4.3 per cent. This result is somewhat lower than that obtained by Du Bois, who found the average percentage loss to be 6.02 per cent. When the results are considered as a whole the conclusion appears to be warranted that fat is almost completely absorbed when given in very large quantity.

THE ABSORPTION OF PROTEIN

The quantity of protein in the diet was kept as nearly uniform as circumstances permitted. The lowest daily average intake of nitrogen was 12.0 gm., the highest was 16.6 gm.

The total nitrogen in the stools varied from 0.84 to 2.89 gm. The average total nitrogen for all stages of the disease amounted to 1.57 gm. The highest average loss, according to periods, of 1.84 gm. a day occurred in the steep-curve stage. The smallest average loss of 1.20 gm. occurred in the stage of continued fever. The quantity of fat in the food appeared to be without influence on the nitrogen loss.

The average percentage loss of nitrogen according to periods varied from 10.7 per cent. to 12.2 per cent. The average percentage loss for all stages of the disease was 11.2 per cent. This result is higher than that obtained by Du Bois, which amounted to 7.1 per cent. No explanation of this difference has been found.

SUMMARY

The feces of seven typhoid patients on the high calory diet have been analyzed for fat and protein in seventeen periods of three to twelve days each in length.

The average total fat loss for all the periods was 6.25 gm., corresponding to a percentage loss of 4.3 per cent. No differences were observed in the percentage absorption of fat in the early and later stages of the fever or up to the end of the first week of convalescence, when the intake was relatively large.

The average total nitrogen loss for all the periods amounted to 1.57 gm., corresponding to a percentage loss of 11.2 per cent.

The constant presence of fat and nitrogen in the feces, even in fasting, vitiates to some extent the validity of the results when expressed in percentages.

CLINICAL CALORIMETRY

SEVENTH PAPER

CALORIMETRIC OBSERVATIONS ON THE METABOLISM OF TYPHOID PATIENTS WITH AND WITHOUT FOOD *

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   E. A comparison of caloric intake and caloric output.
   F. Summary and conclusions.

PREVIOUS INVESTIGATIONS

In a previous communication[1] the respiratory metabolism of typhoid patients as determined by means of the small Benedict respiration apparatus was discussed in detail. The literature of the subject was also reviewed, making repetition here unnecessary. Following this earlier work it was possible to continue the study of the typhoid patients by using the respiration calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital. In the immediately preceding papers of the series[2] the calorimeter and the metabolism ward have been described in detail and data have been given in regard to the normal controls and the absorption of food in typhoid fever. The patients studied were all in the metabolism ward and the calorimeter experiments were conducted in the manner described in the paper on normal controls. In our previous work on the general effect of the high calory diet on respiratory metabolism it was difficult to control the nourishment of the patients so as to determine the basal metabolism and the quantitative effects of different foods. It was, however, pos-

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* From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital, New York.

1. Coleman and DuBois: The Influence of the High Calory Diet on the Respiratory Exchanges in Typhoid Fever, The Archives Int. Med., 1914, xiv, 168.

2. Clinical Calorimetry, Papers 1 to 6, this number. Brief preliminary reports were published in Jour. Am. Med. Assn., 1914, lxiii, 827, and ibid., 1914, lxiii, 932.

sible to demonstrate that the heat production of typhoid patients on a liberal diet was practically the same as that of fasting patients.

Patients with fever have been studied before in various calorimeters. Isaac Ott[3] of Philadelphia as early as 1892 made observations on a patient with malaria using a rather simple type of calorimeter which required a plus correction of 16 per cent. Likatscheff and Avroroff[4] in 1902 made classical experiments on a similar case. In 1909 Benedict and Carpenter[5] studied a few cases of mercurial poisoning with fever in the Middletown calorimeter. An excellent summary of the literature is given in the Russian publication.[4] It is sufficient to say that the rise and fall of body temperature have been ascribed at various times to every possible combination of increase and decrease in heat production and heat elimination. The Russians used the Paschutin calorimeter in which the patient was kept for twenty-two hours, feeding herself and apparently moving about the chamber during the day whenever she felt inclined to do so. The heat elimination was measured in periods of two hours each and the body temperature was determined every two hours, apparently by means of a mercurial thermometer in the axilla. The CO_2 and water elimination were measured in two-hour periods but the oxygen consumption and consequently the respiratory quotient could only be determined by the change in body weight during twenty-two hours. This method seems to have given satisfactory results, since the quotients correspond to those usually found under similar conditions and calculation of the indirect calorimetry in the three experiments gives results which come within —6 per cent. +6 per cent. and +12 per cent. of the direct calorimetry. The Russians themselves calculated the total heat production by adding the calories stored in or lost from the body as the temperature rose and fell to the calories eliminated by means of radiation, conduction and vaporization. They came to the conclusion that the rise of body temperature was due to an increase in heat production. Benedict and Carpenter studied their fever patients under similar conditions, but determined the oxygen, CO_2 and the heat elimination in periods from two to six hours in length. If one takes the periods when their subjects

3. Ott, Isaac: The Modern Antipyretics, Ed. 2, Easton, Pa., 1892; Fever, Its Thermotaxis and Metabolism, New York, 1914.

4. Likatscheff and Avroroff: Investigations of Gaseous and Heat Exchange in Fevers. Reports of the Imperial Military Academy, St. Petersburg, 1902, v, parts 3 and 4. We are indebted to Dr. F. G. Benedict of the Carnegie Nutrition Laboratory for permission to consult his translation of this important work. Excellent abstracts in English have been published in a paper by A. I. Ringer (Physiology and Pathology of Fever, Am. Jour. Med. Sc., 1911, cxlii, 485) and in the monograph on Fever by Ott.

5. Benedict and Carpenter: Preliminary Observations on Metabolism During Fever, Am. Jour. Physiol., 1909, xxiv, 203.

had a body temperature of 38 C. or over and calculates the indirect calorimetry, using the oxygen and quotients, it is easy to determine the divergence of the direct from the indirect calorimetry. The percentage differences are as follows: +5. +10. —9 +9. +2.

METHODS USED

The present work with the calorimeter was undertaken to extend the previous observations and clear up some doubtful points which could be settled only by a most careful control of the diet and by a comparison of the direct and indirect calorimetry. The fact that it was impossible to bring typhoid patients into nitrogen equilibrium unless the diet greatly exceeded the heat production as calculated from the oxygen consumption, suggested the possibility that the method of calculating the indirect calorimetry might be incorrect. There remained also the old work on fever in which abnormally low respiratory quotients were obtained, leading several investigators to believe that the metabolism in fever was radically different from that in health. Finally, it was hoped that it would be possible to determine whether the rising body temperature was due to an increasing heat production or to a decreasing heat elimination.

The subjects studied were typhoid patients who entered Bellevue Hospital in 1913 and 1914. There was some selection of cases in an effort to obtain men in the early stages of the disease who were intelligent enough to cooperate. Most of the patients were taken to the metabolism ward so early in the disease that it was impossible to predict whether the fever would run a mild or severe course. Several patients were transferred from the First Medical Division through the kindness of Dr. Norrie and Dr. Miller to whom we are much indebted.

All of the patients were put on the high calory diet described in previous publications[6] and trained to take the large amounts of food. The very large amounts formerly given to some patients were not administered and the calories seldom exceeded 3,000 a day. An attempt was made to keep the food nitrogen at 15 grams. The stools exceeded two a day only on the occasions mentioned in the histories, and there was seldom abdominal distention. None of the patients was tubbed, although cold sponges were occasionally given to make the patient

6. Shaffer and Coleman: Protein Metabolism in Typhoid Fever, The Archives Int. Med., 1909, iv, 538-600; Coleman: Diet in Typhoid Fever, Jour. Am. Med. Assn., 1909, liii, 1145; The High Calory Diet in Typhoid Fever — A Study of One Hundred and Eleven Cases, Am. Jour. Med. Sc., 1912, cxliv, 659; DuBois: The Absorption of Food in Typhoid Fever, The Archives Int. Med., 1912, x, 177; Coleman: Weight Curves in Typhoid Fever, Am. Jour. Med. Sc., 1912, cxliv, 659; Diet and Metabolism in Fever, Trans. Fifteenth Internat. Cong. on Hyg. and Demog., 1912.

feel more comfortable when the temperature reached 104. Nervous symptoms were not prominent in any case, although one or two of them were mildly delirious for a few days. Most of the patients were cheerful throughout their illness and read the daily papers. It is estimated that their activity increased their metabolism about 10 per cent. above the basal level, although this figure is necessarily only an approximation.

CASE REPORTS

Case 1.—Morris S. (severe typhoid) tailor, English Hebrew of Russian extraction, 21 years old, admitted October 17, discharged January 30.

History.—Previous history unimportant; patient is not alcoholic. He landed from England Sept. 28, 1913. October 10 he began to suffer from pain in his abdomen, chest and back. On the thirteenth he had a nose bleed. Since the onset of symptoms he has had no appetite and has been constipated.

Physical Examination.—Patient is a well-nourished young man of small frame and short stature, being 164 cm. tall. There is slight cyanosis of lips and ears, the tongue is heavily coated, tonsils hypertrophied and congested. There is an occasional subcrepitant râle at the apex of the left lung. The spleen is palpable.

Blood taken October 18 gave a negative Widal test but developed a growth of typhoid bacilli. The spleen edge was felt 4 cm. below the costal margin and a few rose spots were present. October 24 the Widal was positive. The next day there were a few sibilant and sonorous sounds over the chest, clearing up by the twenty-seventh. The patient had been on a diet with high carbohydrate and low fat, and on October 23 and 24 had shown abdominal distention with about four liquid stools a day. The distention and diarrhea ceased when the fat was increased and the very large amounts of carbohydrate stopped. For the next month he had only one or two movements a day. October 30 he became a little irrational and his color was grayish, his pulse soft and very dicrotic. November 3 he was irrational in the calorimeter and wrote several notes about the animals which he saw in his hallucinations. The next day he was in much better condition, the pulse was stronger and his physical condition improved steadily.

November 16 the temperature began to rise after it had been practically normal for five days. He felt perfectly well and was bright and cheerful, in spite of a temperature of 104, until the evening of the eighteenth when he had a sharp pain in the right side of the abdomen. This disappeared the next day. This relapse was almost as severe as the original infection, but the patient was not quite so toxic and was never irrational. The temperature remained normal from December 7 to 17. From November 23 to 26 he had frothy stools but these became formed once more when the fat in the diet was increased.

December 17 a second relapse began and lasted until the 27th. During the period of rising temperature he was somewhat apathetic and suffered from headache and was fretful during the two days of high fever. His general condition remained excellent and he never realized that he was having a relapse. Following this, convalescence was rapid, since he had lost practically no weight during his illness. During the next year he reported at the hospital several times, always in excellent condition and five or ten pounds heavier than ever before in his life.

In December, 1914, he returned to the metabolism ward for two days, giving us the opportunity to determine his basal metabolism and the specific dynamic action of the protein meal.

This history is given in detail since Morris S. was placed in the calorimeter twenty-four times. He was an exceptional patient, in that he ate the prescribed diet practically every day and enjoyed the distinction of going in the calorimeter more often than his fellow patients. Nothing made him happier than the extra attention he received on calorimeter days, and as a result he did exactly what he was told to do. We were particularly fortunate in being able to determine the specific dynamic action of protein and the basal metabolism while he was in perfect health, a year after his infection.

Case 2.—Charles F. (severe typhoid), elevator constructor, born in New York, 24 years old, admitted November 4, discharged January 12.

History.—Lives in same house as his nephew Howard F., who has similar symptoms. On October 28 he began to suffer from anorexia, malaise and headache. On November 3 he had a nose bleed. He did not take to bed until admitted to the hospital.

Physical Examination.—Fairly well-nourished young man of medium frame, 166 cm. tall. He is moderately prostrated; there are several rose spots and the spleen edge is palpable 4 cm. below the costal margin.

Blood taken the day after admission gave a positive Widal test and showed a growth of typhoid bacilli. November 7 and again on the eighth he had a small intestinal hemorrhage of about 200 c.c. His general condition remained fair; he was rational and the toxemia not marked. He was given a daily sponge for his high temperature. At this time he took his food very badly and after the hemorrhages ceased it was impossible to give even 2,000 calories. November 14 to 17 he had a severe follicular tonsillitis and his toxemia was marked. Rose spots appeared in crops. On the nineteenth he had a hemorrhage of about 250 c.c. and was very toxic and apathetic for the next week. His pulse was very soft, systolic blood pressure being 95 mm. mercury. By December 3 the temperature was normal, he was much improved and was reading the paper every day. Convalescence was rapid. Throughout the disease he had one formed stool each day.

This patient was very intelligent and was anxious to help us in every way possible but his digestion made it difficult for him to take the food. He was very quiet while in the calorimeter.

Case 3.—Howard F. (typhoid fever of moderate severity), schoolboy, born in New York, 12 years old, admitted November 4; discharged January 22.

History.—Lives in the same house as his uncle, Charles F. He was perfectly well until October 26 when he had a severe headache. On the twenty-eighth he felt so sick that he took to bed. The next day he had a chill; vomited. He had nose bleed on the thirty-first and on the day of admission.

Physical Examination.—Patient is a tall, slender boy who has not yet reached the age of puberty; height 160 cm.; the cheeks are flushed and he looks acutely ill. Heart apex in the fourth space 8.5 cm. to the left of the midline. There are several rose spots on the abdomen; the spleen is not palpable.

On November 14 the blood culture showed typhoid bacilli. November 12 showers of subcrepitant râles appeared at the left base and the next day sibilant and sonorous sounds were heard all over the chest. His general condition was good, and although he was very apathetic, he was perfectly rational. He took his food very poorly, vomiting often. By the seventeenth he was very thin, quite toxic, very drowsy but rational. The pulse was soft but of fair quality.

The sibilant and sonorous sounds persisted until the twenty-fourth, by which time the temperature was falling, the appetite much better and the patient able to read the paper. Convalescence progressed rather slowly. On December 10 he passed two ascarides. The heart action was rapid on exertion and on the eighteenth the apex was in the fourth space 9.5 cm. from the midline. He left the hospital in good condition. Throughout his illness he had one stool a day.

The boy was very intelligent and made a good subject for the calorimeter.

Case 4.—Karl S. (typhoid fever of moderate severity), stoker on steamer to South America, German, 24 years old, admitted December 29; discharged Feb. 18.

History.—Returning on a voyage from Brazil he landed at San Domingo for a few days, reaching New York December 20. Two days later he began to suffer from headache, weakness, lassitude, anorexia and nausea. On the twenty-fourth he began to have daily chills.

Physical Examination.—One hundred and sixty-eight cm. tall, muscular and well nourished. His face is flushed and he looks stuporous. No spots, spleen not palpable. Blood taken the day after admission gave a negative Widal but positive growth of typhoid bacilli. January 1 rose spots appeared and the spleen became palpable. On the third he was prostrated, apathetic and showed slight subsultus tendinum. The pulse was soft and dicrotic and the abdomen distended. When carbohydrates were pushed too high he became distended, but this trouble disappeared when the amounts were decreased. By January 7 he was anxious about his condition and easily frightened. On the tenth his condition was satisfactory and by the twenty-sixth he was afebrile and was reading and studying every day. He was very hungry during his rapid convalescence. February 14 he developed tonsillitis. The temperature rose to 101 and the pulse became rapid. He did not feel sick and resented being confined to bed. On the seventeenth he became insubordinate and was discharged from the hospital. Two weeks later he returned on a visit in good condition.

This patient was a rough sailor of sullen disposition and made a rather restless subject for the calorimeter. During most of the observations on this man one of the water thermometers was being repaired and the method of direct calorimetry could not be used.

Case 5.—Thomas B. (typhoid fever, mild; followed by acute fibrinous pleurisy). Laborer, Irish, 60 years old, admitted October 2, discharged December 8.

History.—Moderately alcoholic. About September 18 began to suffer from malaise, anorexia and fever.

Physical Examination.—Large well-nourished man, who looks acutely ill. He is apathetic and slightly cyanotic.

Blood taken the day of admission gave a positive Widal and showed a growth of typhoid bacilli. Many rose spots appeared but the spleen was never palpable. He took his food well and was never very ill. From October 22 to November 6 the temperature was normal. Then it rose gradually to 104 and fell slowly reaching normal on the twenty-sixth. During this time he developed dulness, bronchial voice and breathing at the left base, the signs being attributed to a pleurisy rather than pneumonia. He made a rapid convalescence.

Case 6.—Richard T. (mild typhoid). Mulatto boy, born in New York, 14 years old, admitted October 6, discharged November 24.

History.—About September 30 began to suffer from headache, weakness, constipation and occasional abdominal pains.

Physical Examination.—Well nourished active boy who has not yet reached puberty. There are a few rose spots and the spleen is palpable.

The day after admission the blood culture gave a positive Widal and showed a growth of typhoid bacilli. The disease ran a mild and uneventful course, in spite of high evening temperatures, until October 25, when he developed slight pain and tenderness over the gall bladder, lasting two days. The temperature reached normal October 29, but rose again in a mild relapse lasting till November 6. Convalescence was rapid.

The boy was somewhat mischievous and was very active throughout his stay in the hospital. While in the calorimeter he spent most of his time looking out of the window and was not as quiet as most of the patients.

Case 7.—Anton K. (mild typhoid), factory worker, Austrian, 18 years old, admitted September 30, discharged November 18.

History.—September 22 he began to have daily chills and fever, lost his appetite, felt exhausted and had severe pains in the epigastrium.

Physical Examination.—This showed a well-nourished man, apathetic and acutely ill. Typhoid bacilli were found in the blood. At the height of his fever he was prostrated and developed slight subsultus tendinum. He took his food well and was in good condition on October 16, the first day of normal temperature.

Case 8.—Rose G. (severe typhoid), born in New York, 12 years old; admitted September 19, discharged November 26.

History.—Menstruation has not yet begun. The girl is tall and very thin and is somewhat deficient mentally. She went through a severe course of typhoid, with marked emaciation. Blood culture showed typhoid bacilli. During the disease she had râles at both bases and developed bed sores because she had all her life been incontinent of urine. Temperature reached normal October 29, and she was up and about on November 17. During convalescence she ate enormous amounts of food, with very slight gain in weight. She was not in the metabolism ward and exact figures for the food were not obtainable, but it seemed as if the discrepancy between food and gain in weight could be accounted for only by a greatly increased metabolism. The first hour she was in the calorimeter she was quiet, but during the second hour she voided in bed and began to cry, making it necessary to end the observation.

Case 9.—Edward B. (severe typhoid), longshoreman, born in Ireland, 36 years old; admitted October 3, 1914, discharged February, 1915.

History.—He remembers no previous illnesses. October 1 he began to suffer from headache, pains all over the body and abdominal cramps, with diarrhea and three to four stools a day. He had no nausea and the appetite was good.

Physical Examination.—Well-nourished man of medium frame, fairly muscular. He is dull and apathetic and moderately prostrated. The heart is rapid, not enlarged, the lungs are clear, abdomen soft, spleen palpable. There are a few rose spots.

The blood on October 4 was sterile, but gave a positive Widal test. On the sixth he was very drowsy; by the tenth he was comfortable and eating well. October 13 the temperature had again risen, the pulse rate had jumped to 120 and the quality of the pulse was poor. On the twentieth he was much better and was taking his food well, but the abdomen was slightly distended. By November 1 the temperature was almost normal and the general condition excellent in spite of a small rapid weak pulse. By November 7 the temperature was up again, and he was beginning to feel indisposed. The appetite was poor and the pulse rate between 138 and 148. During the next few days the pulse was very rapid, slightly irregular, and very weak. He was very toxic but was rational except for short periods when the mind was a little hazy. November 16 he had a small hemorrhage with a short period of collapse, but recovered quickly. His condition improved steadily until December 3 when the temper-

ature rose once more and he suffered from a moderately severe relapse, lasting until December 21. Following this was a period of three days of normal temperature and then a fourth relapse, very mild in character lasting only three days. During the whole period of his illness his nutrition remained good; he was always cheerful and read the newspaper almost every day.

Case 10.—John K. (typhoid fever, mild), deck hand, Polish, aged 35; admitted Dec. 12, 1914, discharged Jan. 27, 1915.

History.—December 2, began to suffer from malaise. December 5 had a severe chill and took to bed; since then has had chills almost every day. Has had continuous headache, has vomited frequently and has been constipated.

Physical Examination.—Tall and thin, fairly muscular. Tongue dry, coated, fissured. Heart and lungs clear, spleen palpable, many rose spots.

December 12, the blood culture was sterile but the Widal positive. On the thirteenth he had his last chill, on the sixteenth he was apathetic and prostrated, pulse was slow and dicrotic, there was a patch of herpes on the upper lip. As the temperature fell during the next few days his condition improved rapidly, but the apathy remained until the temperature was normal, and he was unusually quiet, remaining almost motionless all day long. Convalescence was rapid.

DISCUSSION OF RESULTS

Law of Conservation of Energy in Fever.—The law of conservation of energy has been shown to apply to the lower animals, to normal men and to babies, and has been discussed in the previous paper (Paper 6) on normal controls, in which it was demonstrated that with normal men a satisfactory agreement between the direct and indirect calorimetry could be obtained in periods as short as one hour. While there are few who doubt that the law applies to men with fever, it may not be superfluous to bring forward proof.

An agreement of the direct and indirect calorimetry within the limits of experimental error indicates that protein, fat and carbohydrate are oxidized to the same or approximately the same end products as in health and that in the oxidation they give off the standard amounts of heat. The method of calculating the indirect calorimetry depends on the assumption that the calories furnished by each gram of protein, fat and carbohydrate correspond to the standard figures of Loewy,[7] protein 4.32, fat 9.46, starch 4.18. The results obtained by the method of direct calorimetry, which is dependent only on fundamental laws of physics, must remain the standard method of comparison when considering large groups of experiments. Once the agreement has been proved for the group, the method of indirect calorimetry is preferable for individual experiments as has been shown in previous papers on account of the technical difficulty of the method of direct calorimetry in short periods.

Table 1 gives a summary of the percentage divergence of the direct and indirect calorimetry in all the experiments on the typhoid patients,

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7. Loewy: Der respiratorische und der Gesamtumsatz, Oppenheimer's Handb. der Biochem, 1911, iv, 280.

the great majority of them being three hours long. In all cases the indirect method was used as a standard. If we consider the total measurement of 12,822 calories, we find the direct method, as calculated from the rectal temperature, gives results only 2.2 per cent. lower than the indirect. In almost half of the experiments the body temperature was measured by a thermometer of two units strapped on the thorax in the region of the apex of the heart and just below the right nipple, each unit being covered by a pad of cotton about 15 cm. square and 4 cm. thick. The rectal thermometer was inserted about 12 cm. beyond the sphincter. In a previous paper attention has been called to the fact that in these typhoid cases in which both methods were tried

TABLE 1.—Percentage Divergence of Direct from Indirect Calorimetry in the Individual Experiments

Percentage Divergence	Number of Experiments Falling in Each Group					
	According to Rectal Temperature			According to Surface Temperature		
	+ Divergence	— Divergence	Total	+	—	Total
0- 5.............	17	22	39	11	7	18
6-10.............	3	15	18	2	7	9
11-17.............	1	3	4	0	1	1
Total.......	..	..	61	..	..	28
Average Error..	..	..	±4.9%	..	..	±4.0%

	Indirect	Direct*	Divergence
Total calories measured in all experiments...........	12,822.03	12,539.67	% —2.2
Excluding first periods..................................	8,470.93	8,488.97	+0.2
Calories measured in febrile experiments excluding all first periods	5,720.21	5,583.55	—2.4

* According to rectal temperature.

slightly better results were obtained by using the surface thermometers to give the temperature changes of the body than by using the rectal. In the long run the rectal thermometer is the more reliable, since it is not so easily displaced by bodily movement, but enough evidence has been accumulated to show that the rectal temperature does not always change in the same degree and not always in the same direction as the average body change. As the body cools off there may be a relative increase in the heat near the surface of the body, since this is the place that most of the heat is dissipated. The opposite takes place when the temperature is rising. On account of the rapid circulation of blood

there is, of course, a tendency for the temperature curves of the different parts of the body to follow the deep temperature as measured in the rectum.

In the sixty-one experiments in which the rectal temperature was measured the average divergence of the indirect calorimetry from the direct calorimetry (as based on the rectal temperature) is only ± 4.9 per cent. In twenty-eight of these experiments it was possible to base the calculations on the changes in the surface temperature, with an average divergence of 4.0 per cent. using this latter method. This divergence of 4 or 5 per cent. is not more than one often finds among normal controls, since the technic is difficult even with trained subjects. The reason for the total minus error of 2.2 per cent. is not clear. The largest part of this error frequently falls in the first hour, especially in patients with fever, and we have been led to suspect that the subject continues to give out heat to the wooden bed frame and to the bedding even after he has been on the bed for an hour. If we excluded from our calculations the first periods, while the calorimeter is still coming into thermal equilibrium, we find that the direct and indirect methods agree within 0.2 per cent. If we consider only those experiments made during the febrile period, we find a larger proportion show a minus error in the direct calorimetry than when we take all the experiments put together. Excluding the first hours of each experiment, however, the direct calorimetry gives a total only 2.4 per cent. lower than the indirect. The difference is so small that it might be found in a group of normal controls. It may be entirely accounted for by the difficulty in measuring the average body temperature during fever.

Basal Metabolism in Typhoid Fever.—In Paper 4 of this series the reasons have been given for the selection of the standard of the average normal basal metabolism. The figure of 34.7 calories per square meter per hour as based on Meeh's formula has been used in all the calculations. It was impossible to use the new surface formula as a standard since this was not devised until most of the typhoid work had been completed.

The relationship of the basal metabolism of the typhoid patients in the various stages of the disease to the normal is shown in Table 2. This corresponds in a striking manner with the averages of the fasting typhoid patients investigated by Kraus, Svenson, Grafe and Rolly and collected by us in a previous publication.[1] It is evident from the general trend of the results that the total metabolism increases and falls in a curve roughly parallel with the body temperature, and that the period when it drops below normal in many patients corresponds with the period of subnormal temperature which occurs so often in the first week of convalescence. From a study of the results obtained by the

calorimeter and by various smaller types of respiration apparatus, it is apparent that there is considerable variation in the heat production of different patients and the same patient at different stages of the fever. While we can state that the average increase in typhoid fever is approximately 40 per cent., we must remember that figures over 50 per cent. are frequently encountered. This should make us cautious in drawing too many deductions from feeding experiments unaccompanied by determinations of the respiratory metabolism. It should also be remembered that typhoid fever is the only fever which has been thoroughly investigated and that if variations occur in this one disease the variations may be quite different in other febrile diseases such as erysipelas, pneumonia, puerperal fever, etc.

TABLE 2.—Basal Metabolism, According to Periods of Typhoid Fever

Periods	Number of Patients	Number of Observations	Average Per Cent. Rise Above Average Normal 34.7 Cal. per Sq. M.	Average Respiratory Quotient
Ascending temperature	2	2	+37	0.79
Continued temperature	5	7	+42	0.77
Early steep curve	3	4	+26	0.82
Late steep curve	3	3	+16	0.82
Relapse— Ascending temperature	2	3	+25	0.82
Continued temperature	2	2	+51	0.76
Early steep curve	2	4	+36	0.78
Late steep curve	1	1	+16	0.79
Convalescence— First week	3	4	−2	0.91
Second week	3	5	+6	0.88
Third week	1	1	+17	0.81
Fourth week	2	2	+15	0.86
Fifth week	2	2	+4	0.81

Benedict and his co-workers in all their recent publications have drawn attention to the fact that pulse rate and total metabolism show curves which are roughly parallel. As might be expected this parallelism is not as apparent in typhoid fever as in the conditions they have studied. Typhoid is characterized by a slow pulse in the first two weeks when the metabolism is high. The experiments here reported do not show any striking agreement in the rise and fall of the two curves.

The Specific Dynamic Action of Food.—When studying the effects of the high calory diet in typhoid fever with the small Benedict respira-

tion apparatus, the writers noted the fact that the metabolism of liberally fed typhoid patients was scarcely raised above the metabolism of fasting typhoid patients. The conclusion was drawn that food exhibits little or no specific dynamic action in typhoid fever. One of the chief objects of the present research was to study this striking phenomenon more closely, inasmuch as some observers, among them Von Noorden,[8] have stated that the specific dynamic action of food was increased in fever, exophthalmic goiter and several other conditions.

We have seldom kept typhoid patients in the calorimeter for periods exceeding three or four hours. After this length of time the patients often become restless and bored, making the results unreliable. This

TABLE 3.—Specific Dynamic Action of Protein and Carbohydrate in Health, Fever and Convalescence

Subjects	Number of Experiments	Average Gm. of Nitrogen or Glucose in Food	Average Gm. Food per Kg. Body Weight Nitrogen or Glucose	Average Per Cent. Rise in Metabolism
Protein meal				
Two normal men*	2	10.1	0.147	9.3
Four febrile patients	6	8.6	0.174	4.5
Four convalescents	5	10.2	0.217	16.6
Commercial glucose				
Three normal men*	3	115.0	1.6	9.1
Two febrile patients	4	115.0	2.2	1.0
Three convalescents	3	115.0	2.7	9.8

* Since the completion of Paper 4 two more normal controls have been given the test meals. Morris S. on Dec. 18, 1914, showed a rise of 6.5 per cent. after a meal containing 9.6 gm. N.; Albert G. on Jan. 6, 1915, showed an increase of 9.0 per cent. in his metabolism after 115 gm. commercial glucose.

has made it impossible to determine the basal metabolism in a two hour experiment and follow it immediately by a three or four hour experiment to find out the effect of food. Moreover, in such a long period the temperature might change several degrees, making the results difficult of interpretation. In the case of normal controls, the basal metabolism is so uniform from day to day that very accurate results can be obtained by determining the basal metabolism and the metabolism after food on different days. In fever the change in the level of metabolism from day to day makes the results less accurate but the error will be small if certain precautions are taken. The level of basal heat production changes in a fairly gradual and uniform curve and

8. Von Noorden: New Aspects of Diabetes, New York, E. B. Treat & Co., 1912, p. 20.

there is but a small change in twenty-four hours unless the temperature or the general condition of the patient changes markedly. For this reason the effect of a given meal has been determined sometimes the day before, sometimes the day after and sometimes the day between basal experiments. The protein meal was given six times in the febrile period and the glucose meal four times. It is against the laws of probability that the basal metabolism should take a sudden change in the same direction on all these days.

The fact that the average amount of protein given in the febrile period was less than that given in health was due to the poor appetite of the patients at the height of the disease. Even in health and in

TABLE 4.—Chart Showing Negative Nitrogen Balances in Typhoid Patients who Receive Food Calories in Excess of Calculated Heat Production

Patient	Dates or Days of Disease Inclusive	Days in Period	Range of Maximum Temperature, Degrees F.	Calculated Heat Production, Cal.*	Food Calories*	Food N, Gm.*	Nitrogen Balance Gm.*
Morris S.	Oct. 23-Nov. 3	12	102.8-104.6	2,266	2,863	16.4	—4.4
	Dec. 19-24	6	101.9-105.1	2,085	2,989	13.2	—2.4
Charles F.	Nov. 28-30	3	101.2-103.4	1,752	2,458	12.0	—4.6
Karl S. ...	Jan. 12-18	7	101.0-105.0	2,197	2,985	16.1	—3.2
	Jan. 19-22	4	98.8- 99.0	1,678	2,819	14.6	—1.9
John K....	Jan. 15-20	6	103.2-104.0	2,568			
Frank W.†	Days of Disease 11-14	4	104.0-105.4	2,200	2,250	11.3	—5.0
	15-19	5	103.0-104.0	2,238	3,320	15.3	—3.3
	20-23	4	101.0-103.6	2,054	2,362	15.9	—1.5

* Figures given are averages for twenty-four hours.
† Taken from Coleman and Du Bois.[1]

convalescence the meal is a large one, containing almost as much protein as most people consume in a day. We must remember also that the normal controls weighed 75 and 63 kg. when they took this meal and that the typhoid patients weighed 51, 58, 35, and 54 kg., respectively. As is shown in Table 3 the controls received less nitrogen per unit of body weight than the fever patients. We can therefore state that protein and glucose exhibit a much smaller specific dynamic action in typhoid fever than in health, while in convalescence from the disease the specific dynamic action seems to be greater than normal. In the case of glucose there was practically no specific dynamic action in fever, and in the case of Morris S. the specific dynamic action of the protein was very slight.

The cause for this phenomenon has not yet been definitely ascertained but the most plausible theory was stated by Dr. Graham Lusk[9] in the discussion on the symposium on nutrition at Atlantic City in 1914. He called attention to the well known fact that if the metabolism be increased by lowering the environmental temperature there may be

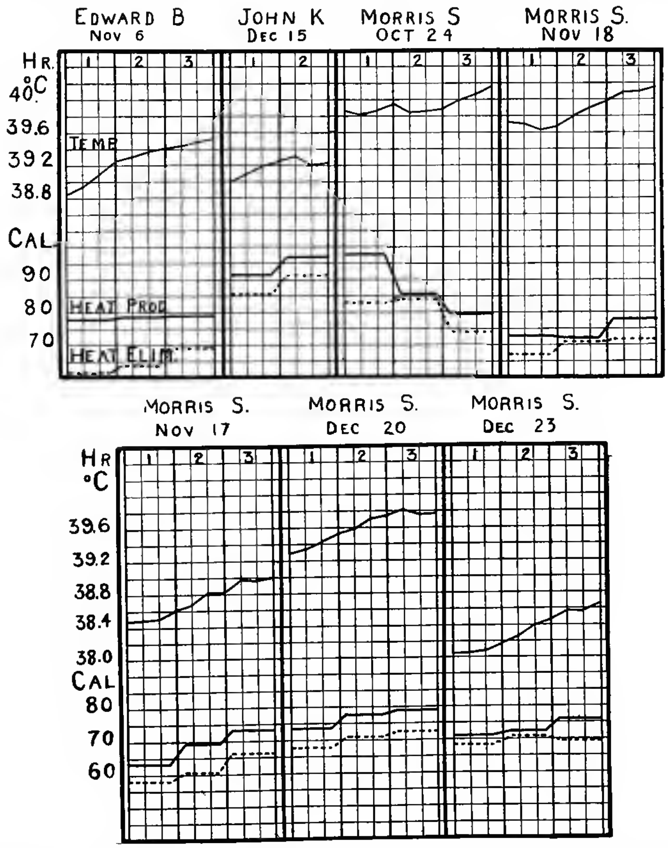

Chart 1.—Curves showing the relationship of heat production and heat elimination in fever. Rising temperature. The uppermost line shows the rectal temperature as measured every twenty minutes. The heavy continued line represents the heat production in hourly periods as determined by the method of indirect calorimetry. The dotted line gives the heat elimination as determined by the measurement of the calories of radiation, conduction and vaporization. The difference between the levels of these two lines represents the heat stored in the body as the temperature rises. Note the fact that in every case except one the heat elimination increases with a rising temperature.

no specific dynamic action as usually induced by ingested food. In like manner if the metabolism be raised in fever, food ingestion may cause no increase. He also stated that since protein metabolism in fever

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9. Lusk: Jour. Am. Med. Assn., 1914, lxiii, 831, foot of page.

can never be reduced to as low a level as is present in the normal organism, therefore protein ingestion in fever often merely serves to replace the protein already breaking up in increased quantity, and such protein ingestion would not then serve to increase the heat production.

The Regulation of Body Temperature.—The study of the regulation of body temperature is one that demands the utmost accuracy of technic. The question at issue is whether a rise in temperature is due to an increase in heat production or a decrease in heat elimination. Previous investigators have tried to solve this problem on data obtained from the direct calorimetry alone, or from the indirect calorimetry accompanied by measurements of body temperature. In either of these two methods the whole calculation would depend on the exact

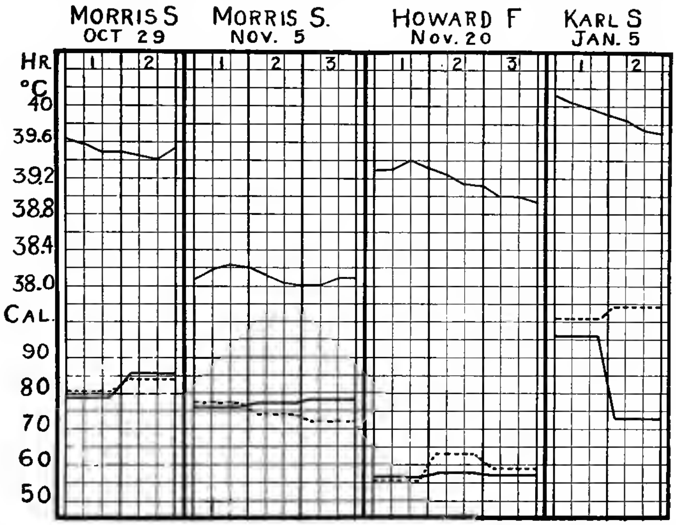

Chart 2.—Curves showing the relationship of heat production and heat elimination in fever. (See legend Chart 1.) Temperature level or falling. In the last two experiments it will be noted that the heat elimination rises above the production.

measurement of the average change in body temperature, the exact calculation of specific heat of the body and the amount of heat stored in or lost from the body. It has been shown in this and preceding papers that these measurements and calculations are the weakest points in the science of calorimetry and it is only very recently that the technic has been so developed that investigators have attempted a comparison of the methods of direct and indirect calorimetry in periods shorter than six to twelve hours, periods obviously too long for the study of the problem in question. If, in a period of experimentation, the results obtained by the method of indirect calorimetry and by the method of

direct calorimetry, using either the rectal or the surface temperature, do not agree within 5 per cent., we must suspect some error, probably in the measurement of the average body temperature change. For this reason we have eliminated from the discussion all experiments in which the two methods do not agree within 5 per cent. It is also preferable to eliminate all experiments after the taking of food and all experiments in which the subject was not quiet. This gives us eleven experiments during the febrile period in which the technic left nothing to be desired.

In Chart 1 are grouped those experiments in which there was a rising body temperature. The dotted line shows the total heat eliminated from the body by means of radiation, conduction and vaporization. The continued line shows the heat production as determined by the method of indirect calorimetry, which does not use a single factor that affects the dotted line. With a rising body temperature the heat production within the body must be greater than the elimination to provide for the storage of heat in the tissues. Many are of the opinion that the rise in temperature is chiefly due to a decrease in the heat elimination. This we find to be the case only in the last hour of one of the seven observations, there being a sharp drop in both heat production and elimination towards the end of the experiment on Morris S. on October 24. In all the other periods the rising temperature was accompanied by an increasing heat production which outweighed the increasing heat elimination.

In Chart 2 which shows periods in which the body temperatures were fairly level the production and elimination were about equal and constant. In the two observations with falling temperature the heat production remained fairly level while the elimination was increased.

Heat Production, Weight and Nitrogen Equilibrium.—In the cases here studied it is possible to make a comparison of the caloric intake and the caloric output. The intake consists of the calories of the food. The output is made up of many factors, but principally of calories lost by radiation, conduction and the evaporation of water. The first and most important consideration is the determination of the basal heat production as measured by the methods of direct and indirect calorimetry. As has been shown above, the two methods agree within 2 per cent. The actual heat production during the different hours of the day can depart from the basal as a result of various factors. We have shown above that the ingestion of large amounts of food causes but a slight increase in metabolism, averaging less than 5 per cent. in the case of protein and only 1 per cent. in the case of carbohydrate. These increases may be considered the maxima since the amounts of foods given were the largest the patient could take and the hours of the

observation were the hours of the greatest specific dynamic action. The exact percentage rise caused by the stimulation of the food taken during the whole day is problematical but may be estimated as about 3 per cent. The percentage of calories lost in the feces has been studied in two previous papers and has been found to be practically normal. The calories lost as urea and in the feces are taken into consideration in the calculation of the fuel values of the food. In the one case in which there was alimentary glycosuria (Frank W.),[1] the calories lost as dextrose have been subtracted from the intake. In a previous paper the writers have discussed the evidence against an abnormal loss of partially oxidized carbon compounds in the urine and have come to the conclusion that this factor is negligible. The entire absence of abnormal respiratory quotients supports this view. The lowest quotient found was 0.72, the highest 1.04, obtained respectively during fasting and high carbohydrate ingestion, and thus exhibiting entirely normal relations.

The most uncertain factor is the variation in heat production caused by changes in the muscular activity. It is quite possible that a patient who is very delirious and very restless might produce twice as many calories as when quiet. The total heat production of such patients could be determined only by the Middletown type of experiment in which the subject was kept in a respiration calorimeter for days at a time. Such experiments are obviously impossible in typhoid fever. The question remains as to whether we obtain a fair sample of the day's metabolism by making two or three observations a week between the hours of 11 in the morning and 2 or 3 o'clock in the afternoon. This period includes some of the morning hours when the metabolism is said to be low and some of the afternoon hours when it is said to be high. During the experiment the activity of the patient has been almost the same as the activity observed in the ward during the greater part of the day between the hours of 5 in the morning and 8 in the evening. In the calorimeter the subjects are allowed to turn from side to side several times during the hour and they shift their position often enough to make themselves comfortable, which is exactly what they do in their beds in the ward. Part of the time they doze and part of the time they are awake and are looking out of the calorimeter window. In the ward they are kept flat in bed and are never allowed to sit up until the temperature has been normal for several days. They are never given cold tubs and hardly ever given cold sponges. Their food is served on trays and they help themselves with a minimum of exertion. In the morning the nurse gives each patient an enema, sponges

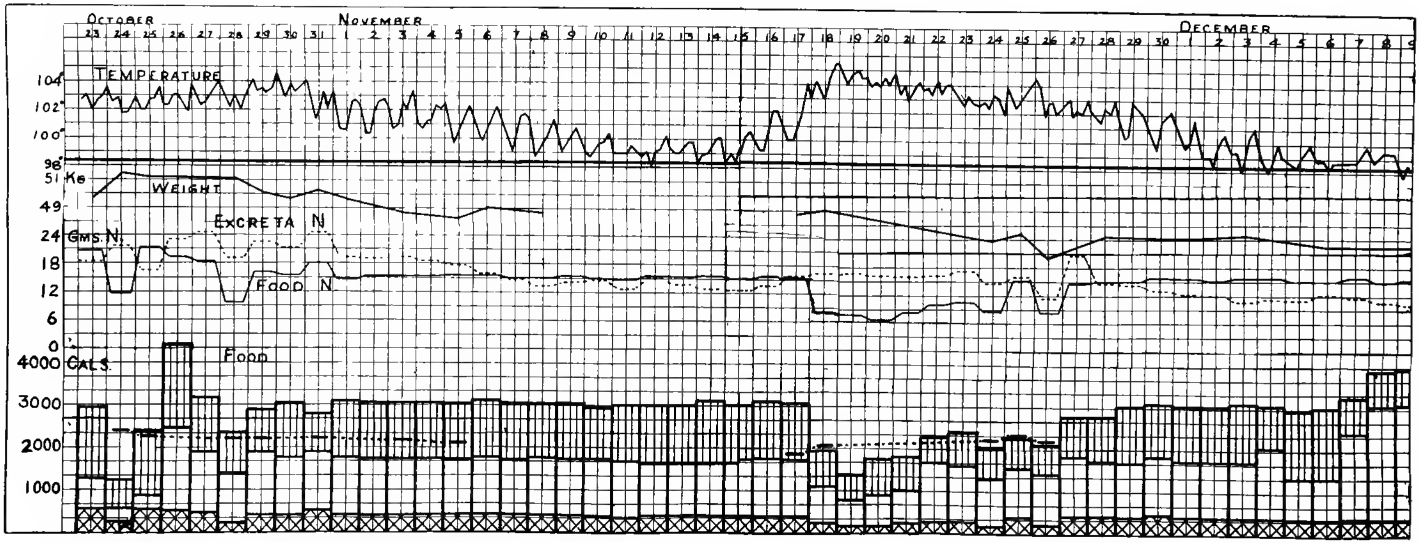

Chart 3.—Part 1

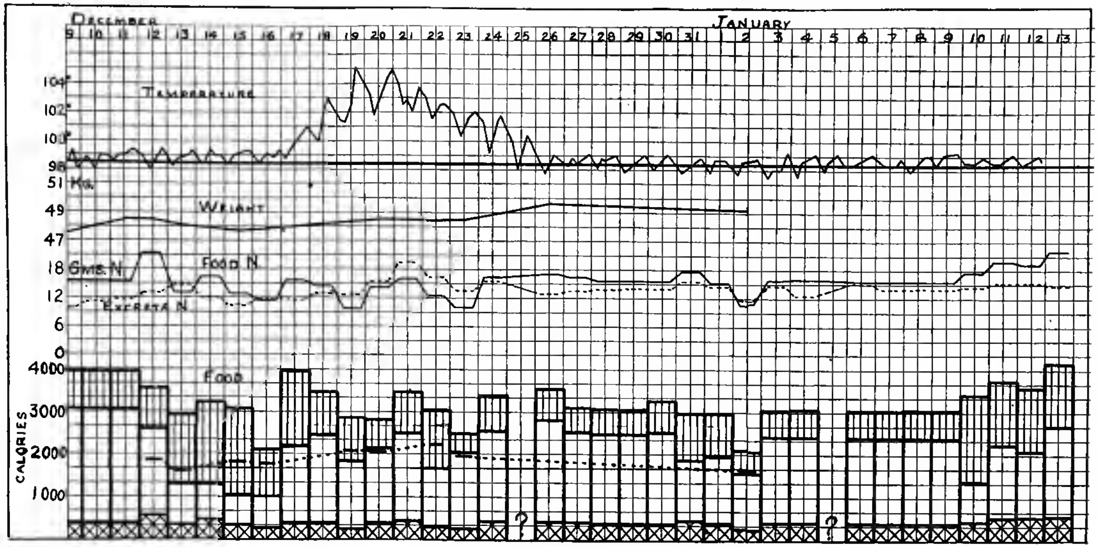

Chart 3.—Part 2

Chart 3.—Morris S.—Temperature, body weight. Food nitrogen, continuous line; excreta nitrogen, dotted line. At the base of the chart, columns representing total calories of food. Protein calories, crossed diagonals — fat calories, blank — carbohydrate calories, vertical lines. The dot-dash line represents the estimated heat production in calories for twenty-four hours. The dashes are placed on days of the observations in the calorimeter. Note that the calories of the food exceed the estimated heat production except for a period during the first relapse. Food was not measured on December 25th and January 5th.

him off with warm water, slides him from his bed to the weighing platform, makes up his bed and slides him back again. During the rest of the day he is seldom disturbed and he spends his time dozing, reading or talking with his neighbors. A few of the patients have been mildly irrational for a few days at a time and such occurrences have been noted in detail in the histories. Subsultus tendinum and jactitation have rarely been observed. On the other hand, there must be a reduction of the metabolism at night since the patients sleep soundly and are seldom disturbed. In a previous paper we have estimated that the bodily activity increases the metabolism during the whole day to an average of 10 per cent. above its basal metabolism. Since that time we have had the opportunity of making two observations on patients who were irrational and restless. November 3 Morris S. was in the calorimeter for three hours. During the first hour he was unusually quiet, during the second hour he was restless and tossed about the bed, during the third hour he was evidently irrational, tossed about and wrote three or four long notes which he held up to the calorimeter window to tell us about the animals that were biting him with their sharp teeth.

In spite of this unusual activity his metabolism during the three hour period was only 43 per cent. above the normal and was only 5 per cent. higher than during the quiet basal observation made two days later, when the temperature was lower. Edward B. on Nov. 10, 1914, was in the calorimeter with a temperature of 40.3 C., and during the second and third hours was restless and mildly irrational. His heat production was only 51 per cent. above the average normal. These two observations, which are fair samples of the severest symptoms observed in the typhoid patients presented in this paper, do not indicate any unusual degree of increase of heat production from the moderate activity. There may be an uneconomical expenditure of energy in typhoid in the performance of a certain task but even so the total expenditure is not great in these cases. It is hoped that at a later date the question of muscular efficiency in fever may be solved by having typhoid patients and normal controls do a stated amount of work on an ergometer while in the calorimeter.

A detailed consideration of all the factors is of importance when one attempts to draw conclusions from a discrepancy between the calculated intake and the calculated output. It is necessary to consider the possible errors in the various determinations and it is necessary to select somewhat arbitrary average percentages for the various factors. The measurement of the food intake is unusually accurate. Most of

the foods such as cereals, bread, sugars, egg white and egg yolk, butter and crackers vary but slightly from the samples analyzed. The other foods given, such as milk, cream, and dried apples are not subject to large enough variations to affect the results. Foods subject to significant variations are carefully avoided.

The methods of preparation and weighing have been described in another paper and they are believed to be accurate within 2 per cent. It is doubtful if this error combined with the error in the variation of the individual foods exceeds plus or minus 5 per cent. and there is no factor to throw the error on one side of the scale more often than on the other. The heat production of the patients as determined by the method of indirect calorimetry is not subject to an error of more than 1 or 2 per cent. on the average, although it is possible that some individual observations may show an error of 5 per cent. The collection of the twenty-four hour specimens of urine and the estimation of

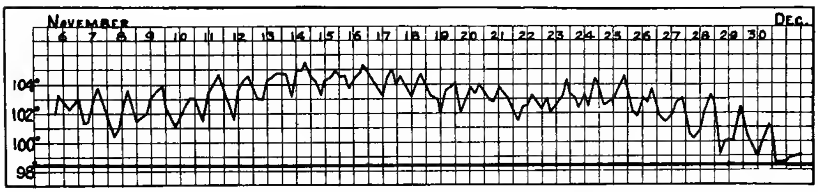

Chart 4.—Charles F. Temperature curve.

the nitrogen are so carefully controlled by duplicate analyses and checks in the collection of specimens and in the calculations that there is no chance for an error greater than 1 per cent. In the cases in which the feces were not analyzed the method of estimating the feces nitrogen as 10 per cent. of the food nitrogen gives a plus or minus error of less than half a gram a day while there is possibly as great an error in the fact that we do not take into account the nitrogen losses through the skin.

In order to estimate the caloric output of typhoid patients on whom respiration experiments were made, one can add to the basal metabolism on average 3 per cent. for the specific dynamic action of the food and 10 per cent. for muscular activity. We can, therefore, calculate with reasonable accuracy the heat production for the day by adding 13 per cent. to the figures obtained in the febrile basal experiments and 10 per cent. to the figures obtained in the experiments after food. In the cases in which several observations were made it seems fair to plot a smooth curve and consider that the heat production of the non-experi-

mental days was the same as on the days in which actual determinations were made.

If we look now at Table 4 and Charts 3, 6 and 8, it becomes evident that three of the patients reported in this paper and one reported in a previous paper[1] showed a distinct negative nitrogen balance when they were receiving considerably more calories than were sufficient to cover the calculated heat production. A glance at the food charts will show that the typhoid patients were given 12 to 16 grams of nitrogen a day and that the proportions of fat and carbohydrate were well balanced. The only criticism of the manner of feeding is that on the days of the basal determinations it was necessary for the patient to fast sixteen to twenty hours. One might expect a slight negative nitrogen balance at such times, but this should be offset by a positive balance the next day. As a matter of fact the negative balance is not much greater on the experi-

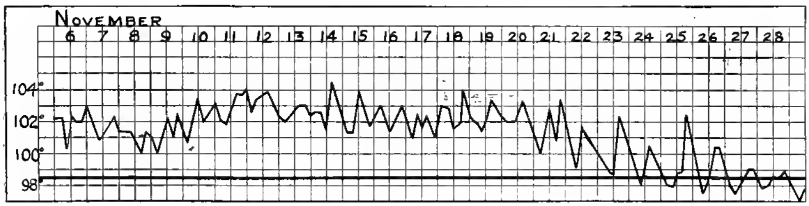

Chart 5.—Howard F. Temperature curve.

mental days. Moreover, as was pointed out in the previous paper, many patients who have not been the subject of respiration experiments have shown a persistent negative nitrogen balance on a diet much greater than the estimated heat production and have not come into nitrogen equilibrium until the theoretical requirement was exceeded by from 50 to 110 per cent.

In another place[1] when touching on this subject we referred to the possibility of a storage of fat while there was a negative nitrogen balance and loss of body weight. The body weight is notoriously a poor index of gain or loss of body tissue except in long periods of observation. The body changes its content of water so easily and so rapidly with changing diets and changing periods of the disease that it would be very easy to store 1 or 2 kilograms of fat without noticeable effect on the weight. We must remember that 1 kilogram of fat represents about 9,300 calories. Even without assuming a change in the water concentration of the body, it is possible to account for the storage of the excess calories. In the tables one can find several periods of almost con-

stant body weight when the patient was losing nitrogen. If we consider that for every 3 grams of nitrogen lost the patient loses about 100 grams of muscle tissue, it is possible to calculate the total muscle tissue lost. If this were replaced by fat the weight would remain constant and the storage of the excess calories could easily be accounted for. For example, Morris S. between October 23 and November 3 lost about 1,770 grams of muscle tissue, which could be replaced by enough fat to represent 15,900 calories.

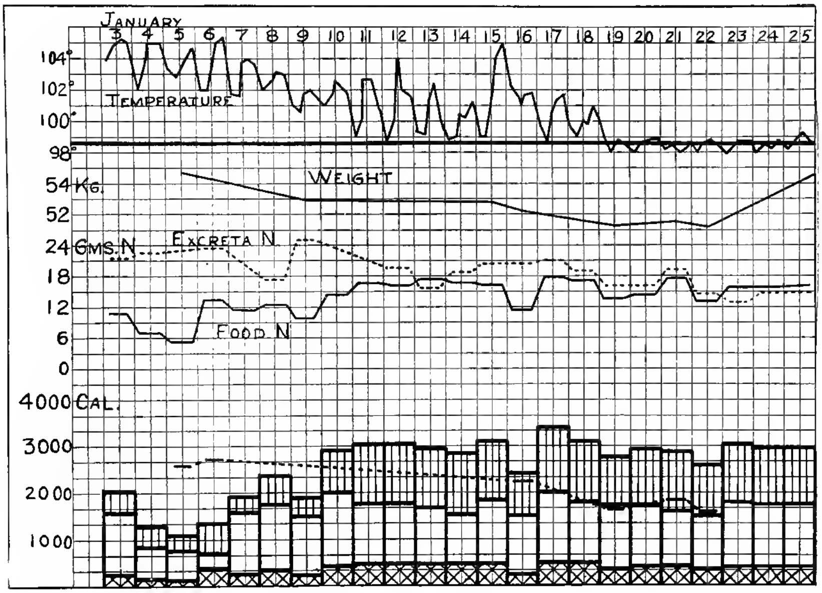

Chart 6.—Karl S. Temperature and body weight. Food nitrogen, continuous line; excreta nitrogen, dotted line. The columns at base represent calories in food. Protein calories crossed diagonals, fat calories blank, carbohydrate calories vertical lines. Dot-dash line represents the estimated heat production in calories for twenty-four hours, dashes being placed on the days of the calorimeter observations. Note the negative balance during the last days of the fever when the patient was receiving in food more calories than the estimated heat production.

In none of the cases were the protein and carbohydrate calories together sufficient to cover the heat production, so it is not necessary to assume the transformation of carbohydrate into fat, although we have shown that this is possible during fever in one patient[1] (Salvatore L.).

The Toxic Destruction of Protein.—The proof of the fact that typhoid patients show a negative nitrogen balance on a diet which furnishes more calories than the heat production, is perhaps the most

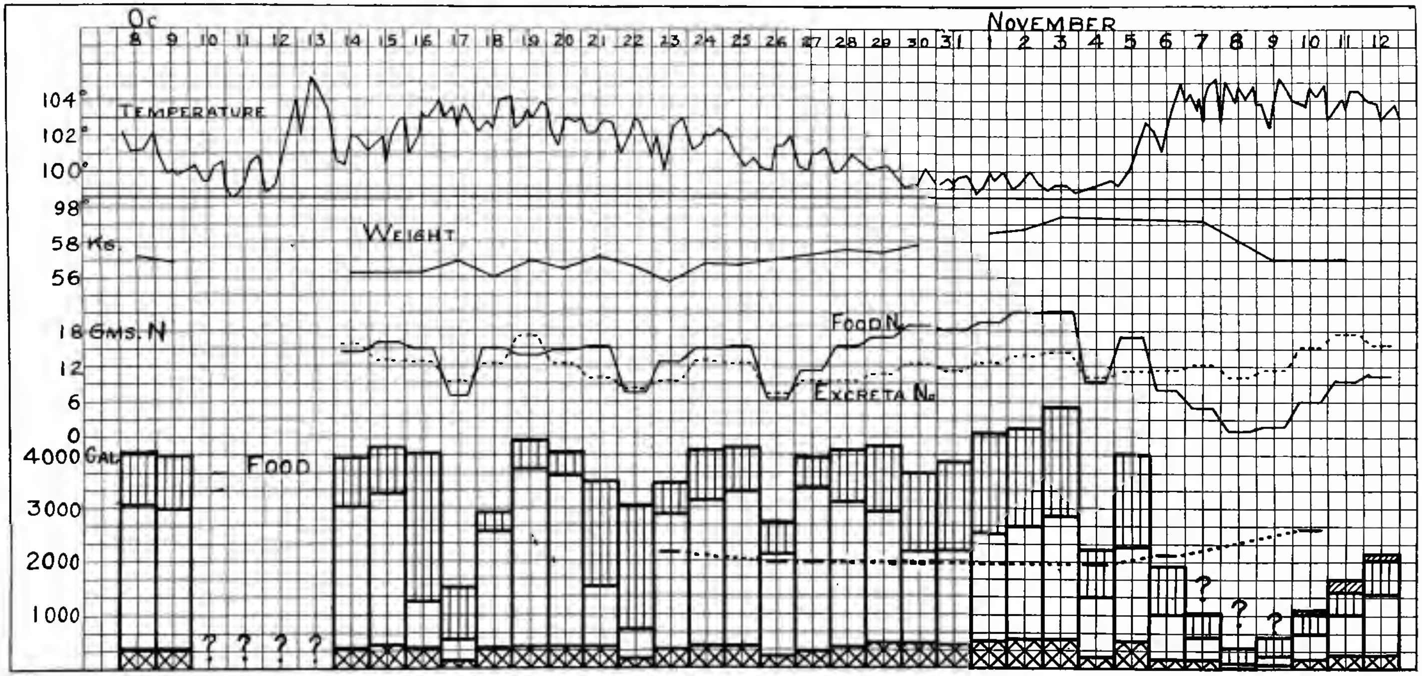

Chart 7.—Edward B. Temperature, body weight, food and excreta nitrogen. Food calories and dot-dash line representing estimated heat production. On November 7th, 8th and 9th, patient vomited, making measurement of food intake somewhat inaccurate. November 10th, 11th and 12th he received some alcohol calories.

important piece of evidence which has yet been presented in the discussion of the so-called toxic destruction of protein. Clinicians have long been aware of the large excretion of nitrogen in fever and have attributed it to an abnormal destruction of protein caused by the toxins of the disease. It is not necessary in this connection to review the older clinical work, since that is admirably presented in the standard discus-

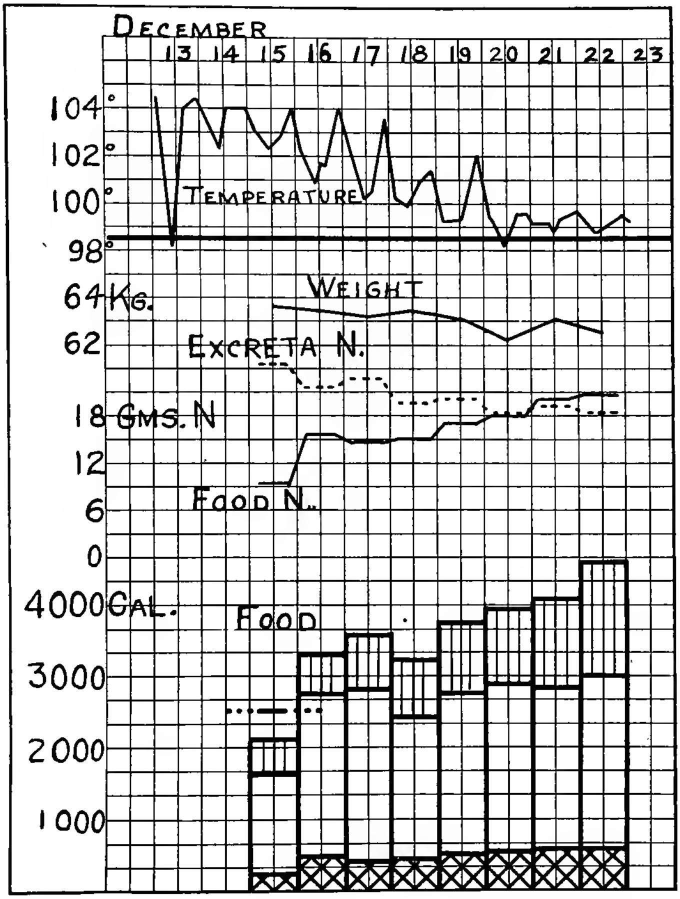

Chart 8.—John K. Temperature, body weight, food and excreta nitrogen. Food calories and dot-dash line showing estimated heat production.

sions of metabolism in fever. The results of the large number of investigations made on lower animals, while important, cannot with certainty be transferred to man.

The question of the toxic destruction of protein took on a new aspect when in 1909 Shaffer and Coleman[6] showed that it was possible

to obtain nitrogen balance in typhoid patients, even during the second and third weeks of the disease. This they accomplished only by making the total caloric value of the food very high, from 60 to 90 calories per kilogram, and the food nitrogen from 9 to 15 grams. In their discussion of the results they expressed the opinion that "....it is perhaps improbable that the total heat production reached the values represented by the larger amounts of food." This work proved that there was no toxic destruction in the sense of a nitrogen loss which could not be counterbalanced by the nitrogen intake.

The question of the average heat production of typhoid patients was fully discussed in last year's paper[1] and attention was drawn to the fact that typhoid patients did not come into nitrogen equilibrium until their theoretical caloric requirement was exceeded by from 50 to 110 per cent. Grafe[10] in 1911 had shown that his typhoid patients when studied in a respiration chamber, ten to sixteen hours after their last meal, derived about 10 to 20 per cent. of their calories from protein, a percentage usually found in normal men. From this Grafe concluded that he had shown that the protein metabolism in fever was not abnormal. The percentage of calories derived from protein on the first eighteen hours after food ingestion depends largely on the previous level of the protein metabolism. Normal individuals who have been taking 15 to 19 grams of nitrogen a day will naturally derive about 15 to 20 per cent. of their calories from protein as is shown in Paper 4 of this series. Normal individuals who have been maintaining themselves in nitrogen balance on 4 to 5 grams a day will derive only 5 per cent. of their calories from protein. The comparison should have been made between normal men and typhoid patients while both were on their nitrogen minima. This will be shown later in a discussion of Kocher's work.

Rolland[11] working under Grafe's direction brought several fever patients into nitrogen balance by means of a caloric intake which she believed to be equal to the heat production as estimated from the averages of other patients. Respiration experiments were not made on the patients themselves. Our reasons for believing that the food intake was above the requirement have been set forth in another place[1] (p. 38).

Recent work from Friedrich Müller's clinic has thrown important light on the subject. Graham and Poulton[12] established themselves

10. Grafe E.: Untersuchungen über den Stoff- und Kraftwechsel im Fieber, Deutsch. Arch. f. klin. Med., 1911, ci, 209.

11. Rolland, Anne: Zur Frage des toxogenen Eiweisszerfalls im Fieber des Menschens, Deutsch. Arch. f. klin. Med., 1912, cvii, 440.

12. Graham and Poulton: Influence of Temperature on Protein Metabolism, Quart. Jour. Med., 1912, vi, 82.

on a minimal nitrogen elimination of 4 to 5 grams a day and found no increase in the elimination when they raised their temperatures to about 40 C. by means of a steam bath. Kocher[13] in two normal subjects established a nitrogen minimum at a similar level and found no increase when he raised the heat production by means of a 60 kilometer walk. All of these experiments were made on a caloric intake calculated to cover the requirement. They indicate that rise in temperature alone or increase in heat production alone will not cause an increased protein metabolism, at least when applied for a portion of one day. Kocher then attempted by means of a diet amply sufficient to cover the calculated requirement to bring down the nitrogen elimination of fever patients to the low level obtained in normal men. This he found to be impossible until the active stage of the disease was passed. Grafe[14] in a recent paper has criticized these experiments.

To all of the patients in Table 4 food was given which had an energy content much greater than the amount required by the patients as measured directly when they were in the calorimeter. Although the protein content of the diet, as represented by an intake of 15 grams of nitrogen, was ample to establish nitrogen equilibrium had the diet been given to normal men, it did not accomplish this in typhoid fever. It is difficult to see in this anything except the proof that there is an abnormal destruction of protein in typhoid fever. In some cases the protein destruction continued several days after the temperature had reached a low level. It is impossible to escape the conclusion that the destruction of protein is caused by the toxins of the disease.

SUMMARY AND CONCLUSIONS

The heat production of typhoid patients has been measured by the methods of direct and indirect calorimetry in a series of sixty-one experiments. The two methods agreed closely, the total divergence being 2.2 per cent. and the average divergence in the individual experiments being 5 per cent. This and the entire absence of abnormal respiratory quotients indicate that in typhoid fever protein, fat and carbohydrate are oxidized to the same or approximately the same end products as in health, and in their oxidation give off the standard

13. Kocher, Rudolph A.: Ueber die Grosse des Eiweisszerfalls bei Fieber und bei Arbeitsleitstung, Deutsch. Arch. f. klin. Med., 1914, cxv, 82.

14. Grafe, E.: Zur Genese des Eiweisszerfalls im Fieber, Deutsch. Arch. f. klin. Med., 1914, cvi, 328.

TABLE 5.—CLINICAL—

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo-rimetry, Cal.	Heat Elimi-nated, Cal.	Direct Calo-rimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Morris S. ...... Oct. 24, '13 51.50 kg.	Prelim.	11:35	.....	.....	..	.....	.....	.....	.....	.....	39.86
	1	12:35	30.06	30.02	.73	47.84	0.713	97.69	83.41	84.28	39.95
	2	1:35	27.82	28.13	.77	46.72	0.713	85.89	84.68	81.00	39.89
	3	2:35	26.20	24.04	.79	39.48	0.713	79.28	74.63	85.72	40.17
Morris S. ...... Oct. 25, '13 51.22 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.21
	1	12:00	29.65	26.82	.80	42.10	0.671	88.95	78.03	90.06	39.49
	2	1:00	28.63	25.87	.81	39.10	0.671	85.77	80.11	88.09	39.69
	3	2:00	31.75	25.46	.91	42.82	0.671	86.62	90.07	78.55	39.49
Morris S. ...... Oct. 28, '13 51.50 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.62
	1	12:10	34.12	28.35	.88	43.31	0.732	95.71	92.00	75.53	39.27
	2	1:10	32.64	24.82	.96	42.41	0.732	85.31	94.67	76.33	38.87
	3	2:10	30.25	22.89	.96	39.40	0.732	78.60	86.73	84.65	38.81
	4	3:10	29.93	24.33	.90	34.39	0.732	82.34	78.47	93.97	39.20
	5	4:10	28.38	22.05	.94	31.75	0.732	74.59	74.35	90.84	39.65
Morris S. ...... Oct. 29, '13 49.86 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.63
	1	12:10	26.75	23.77	.82	33.11	0.658	79.00	81.19	76.49	39.50
	2	1:10	27.49	25.95	.77	34.03	0.658	85.28	84.48	85.73	39.54
Morris S. ...... Oct. 31, '13 50.28 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.06
	1	12:00	28.96	25.45	.83	32.13	1.058	84.11	74.09	58.27	38.94
	2	1:00	29.69	24.17	.89	36.41	1.058	81.15	79.19	79.96	39.08
	3	2:00	29.67	26.58	.80	36.76	1.058	87.50	77.70	87.13	39.43
Morris S. ...... Nov. 3, '13 48.53 kg.	Prelim.	10:30	.....	.....	..	.....	.....	.....	.....	.....	38.63
	1	11:30	24.91	20.42	.89	28.58	0.499	69.20	56.44	72.99	39.05
	2	12:30	28.70	26.23	.80	33.10	0.499	83.77	74.39	77.80	39.15
	3	1:30	27.53	27.90	.72	42.11	0.499	90.92	86.25	71.74	38.81
Morris S. ...... Nov. 5, '13 48.45 kg.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	38.08
	1	12:20	25.42	23.10	.80	29.99	0.491	76.70	77.98	81.34	38.19
	2	1:20	26.42	23.05	.83	38.62	0.491	77.19	74.75	67.00	38.01
	3	2:20	25.60	23.65	.79	39.13	0.491	78.29	72.89	75.34	38.10
Morris S. ...... Nov. 17, '13 47.99 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	38.48
	1	12:10	21.90	19.01	.84	24.39	0.336	63.87	57.98	62.77	38.61
	2	1:10	23.58	20.82	.82	24.44	0.336	69.76	60.70	69.71	38.82
	3	2:10	23.79	22.28	.78	26.06	0.336	73.79	66.08	72.85	39.00
Morris S. ...... Nov. 18, '13 48.77 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.72
	1	12:00	24.40	22.01	.81	26.55	0.567	73.01	67.36	64.94	39.67
	2	1:00	26.37	21.38	.90	28.15	0.567	72.56	71.66	82.60	39.98
	3	2:00	25.91	23.57	.80	28.88	0.567	78.11	72.05	77.47	40.15
Morris S. ...... Nov. 24, '13 46.69 kg.	Prelim.	11:13	.....	.....	..	.....	.....	.....	.....	.....	39.54
	1	12:13	29.17	25.27	.78	29.24	0.514	83.56	67.50	68.12	39.59
	2	1:13	26.91	24.54	.75	32.68	0.514	85.26	75.16	64.72	39.33
	3	2:13	26.41	25.48	.75	35.00	0.514	83.64	80.48	73.52	39.16

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	96(?)	36.0	.71	24	75	1	1.90	57.33	Basal.
.....	96	21.0	.77	28	58	14	1.67	50.40	
.....	105	17.0	.79	31	49	20	1.54	46.53	
.....	101	30.0+	.80	20	54	26	1.74	52.36	9:30-10:00 a. m., protein meal. 9.0 gm. N.
.....	96	21.5	.81	21	52	27	1.68	50.48	
.....	105	18.0++	.94	21	17	62	1.69	50.98	
.....	119	35.0	.90	20	29	51	1.88	66.70	At 10:22, 115 gm. com. glucose = 100 gm. dextrose. Asleep from 3-3:40.
.....	113	25.0+5?	1.01	23	..	77	1.68	50.54	
.....	108	30.5	1.02	25	..	75	1.65	46.56	
.....	108	18.0	.93	24	19	57	1.62	48.78	
.....	107	9.0	.99	26	3	71	1.47	44.19	
.....	105	24.0	.82	22	47	31	1.58	47.17	Basal.
.....	106	17.5	.76	20	65	15	1.70	50.91	
.....	101	10.0 (?)	.84	33	36	31	1.68	50.16	8:40-9:20, protein meal; 10.3 gm. N.
.....	102	11.2+	.95	35	12	53	1.62	48.39	
.....	98	9.5	.81	32	44	24	1.74	52.18	
.....	106	11.7	.91	19	25	56	1.42	42.09	Basal. 1st. hr. quiet, 2d. hr. restless, 3d. hr. restless; wrote 3 or 4 notes.
.....	111	32.0	.79	16	59	25	1.71	50.96	
.....	106	8.0+	.70	16	85	..	1.86	55.30	
.....	98	5.5	.80	17	56	27	1.58	46.89	Basal.
.....	109	8.0	.84	17	45	38	1.59	47.18	
.....	112	8.0	.78	17	61	22	1.62	47.86	
37.29									
37.52	100	11.0	.84	14	45	41	1.33	39.28	Basal.
37.83	113	6.8	.83	13	51	36	1.45	42.90	
37.94	112	3.0	.77	12	68	20	1.54	45.38	
38.89									
38.98	114	0.3	.81	21	52	27	1.50	44.44	Basal.
39.27	117	14.7	.92	21	20	59	1.49	44.16	
39.16	124	13.7	.80	19	55	26	1.60	47.54	
.....	...	12.0	.78	16	64	20	1.77	52.32	Basal.
.....	122	0.0	.74	16	73	11	1.81	53.39	
.....	126	0.5	.74	16	73	11	1.78	52.37	

TABLE 5.—CLINICAL CALORIMETRY—

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen. Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Morris S. ...... Nov. 25, '13 47.24 kg.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	39.40
	1	12:20	28.17	24.45	.84	29.86	0.618	81.79	71.86	66.66	39.30
	2	1:20	30.38	26.92	.82	47.61	0.618	89.78	91.51	78.22	38.97
	3	2:20	29.26	27.94	.78	48.78	0.618	89.93	88.95	95.35	39.13
Morris S. ...... Nov. 26, '13 46.11 kg.	Prelim.	10:50	.....	.....	..	.....	.....	.....	.....	.....	39.61
	1	11:50	26.29	24.80	.77	27.88	0.329	82.10	69.08	52.60	39.19
	2	12:50	25.68	24.64	.76	34.79	0.329	81.28	79.19	71.14	38.99
	3	1:50	25.70	24.85	.75	42.13	0.329	81.84	88.38	79.59	38.77
Morris S. ...... Dec. 12, '13 48.61 kg.	Prelim.	10:56	.....	.....	..	.....	.....	.....	.....	.....	37.01
	1	11:56	23.45	20.22	.84	18.48	0.272	68.20	61.73	53.71	36.82
	2	12:56	23.88	20.96	.83	21.26	0.272	70.44	64.58	69.48	36.95
	3	1:56	24.99	21.42	.85	24.01	0.272	72.36	66.64	69.52	37.03
Morris S. ...... Dec. 13, '13 48.07 kg.	Prelim.	10:36	.....	.....	..	.....	.....	.....	.....	.....	37.07
	1	11:36	18.99	16.89	.82	18.84	0.323	56.39	58.07	50.93	36.90
	2	12:36	20.10	17.29	.85	19.31	0.323	58.16	58.63	63.06	37.02
	3	1:36	20.76	18.90	.80	20.26	0.323	62.88	61.95	63.59	37.07
Morris S. ...... Dec. 15, '13 48.17 kg.	Prelim.	10:52	.....	.....	..	.....	.....	.....	.....	.....	37.30
	1	11:52	24.51	18.29	.98	18.41	0.384	63.45	58.74	47.60	37.03
	2	12:52	26.76	18.98	1.03	20.90	0.384	66.42	63.52	64.97	37.10
	3	1:52	26.83	18.82	1.04	22.07	0.384	65.97	64.19	67.97	37.23
Morris S. ...... Dec. 16, '13 47.86 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.32
	1	12:06	22.51	17.81	.92	20.83	0.299	61.10	63.36	61.62	37.30
	2	1:06	21.91	18.33	.87	21.42	0.299	62.12	62.76	63.36	37.33
	3	2:06	22.37	19.33	.84	21.79	0.299	65.08	63.87	60.35	37.25
Morris S. ...... Dec. 19, '13 48.74 kg.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.19
	1	12:10	27.38	21.99	.91	22.55	0.493	74.94	70.40	67.95	39.14
	2	1:10	30.04	22.70	.96	25.64	0.493	78.51	75.00	84.00	39.41
	3	2:10	29.47	23.61	.91	27.26	0.493	80.32	74.21	87.13	39.75
Morris S. ...... Dec. 20, '13 48.52 kg.	Prelim.	10:40	.....	.....	.	.....	.....	.....	.....	.....	39.29
	1	11:40	23.69	22.51	.77	23.81	0.547	73.93	67.11	76.36	39.53
	2	12:40	25.60	23.42	.80	25.60	0.547	77.57	70.95	78.45	39.76
	3	1:40	26.51	23.84	.78	27.47	0.547	78.68	72.88	72.56	39.77
Morris S. ...... Dec. 22, '13 48.87 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	38.65
	1	12:36	37.28	28.77	.94	37.28	0.705	98.85	97.57	112.39	39.05
	2	1:36	28.84	22.32	.94	28.28	0.529	76.65	73.08	88.65	39.47
	3	2:36	28.86	22.21	.95	29.24	0.529	76.39	74.60	78.88	39.59
Morris S. ...... Dec. 23, '13 48.60 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	38.04
	1	12:06	23.51	21.45	.80	25.82	0.428	71.21	68.75	73.19	38.16
	2	1:06	23.94	21.92	.80	25.39	0.428	72.73	70.84	80.86	38.46
	3	2:06	24.35	22.79	.78	25.38	0.428	75.32	69.85	76.84	38.66
Morris S. ...... Jan. 2, '14 49.26 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	36.97
	1	12:16	19.10	16.62	.84	19.75	0.386	55.63	58.53	52.15	36.85
	2	1:16	19.27	17.07	.82	20.20	0.386	56.94	57.89	64.93	37.05
	3	2:16	19.80	18.38	.78	22.05	0.386	60.77	61.64	60.88	37.07

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg	Per Sq. M.	
38.37									
38.66	112	18.6	.85	20	42	38	1.72	50.83	9.35:10:15, protein meal; 8.7 gm. N. Began to sweat at end of second hour.
38.12	122	12.2	.83	18	49	33	1.89	65.80	
37.76	119	9.5	.78	18	62	20	1.90	55.89	
38.87									
38.59	112	5.5	.77	11	70	19	1.79	51.83	Basal. Patient restless in second period.
38.18	119	11.0+	.76	11	75	14	1.77	51.31	
37.53	123	12.0	.76	11	77	12	1.78	51.67	
35.60									
35.52	91	3.8	.85	11	46	43	1.40	41.59	9:03-9:30, protein meal; 10.6 gm. N.
35.69	94	18.6	.83	10	51	39	1.46	42.95	
35.73	98	14.5	.85	10	45	45	1.49	44.12	
35.82									
35.64	74	9.0	.82	15	52	33	1.17	34.64	Basal. Asleep in first period.
35.82	88	9.2	.85	15	43	42	1.21	35.73	
35.98	87	7.5	.80	14	59	27	1.31	38.62	
35.98									
35.54	83	6.0	1.01	16	..	84	1.32	38.95	At 10:13, 115 gm. commercial glucose.
35.72	102	6.1	1.07	15	..	85	1.38	40.77	
35.75	100	1.2	1.09	15	..	85	1.37	40.50	
35.99									
35.93	84	5.7	.94	13	18	69	1.28	37.65	Basal.
35.95	87	2.5	.88	13	35	52	1.30	38.27	
36.00	93	7.0	.85	12	46	42	1.36	40.10	
37.52									
37.29	105	0.3	.93	17	20	63	1.54	45.64	At 10:26, 115 gm. commercial glucose.
37.64	121	7.3	1.00	17	1	82	1.61	47.81	
37.71	121	2.0	.94	16	19	65	1.65	48.92	
37.49									
37.59	108	1.6	.76	20	67	13	1.55	45.13	Basal.
37.87	114	8.1	.79	19	57	24	1.63	47.36	
37.91	117	2.2	.77	18	64	18	1.65	48.00	
36.85									
37.44	109	9.2	.98	19	6	75	1.52	45.07	At 10:24, 115 gm. commercial glucose. First period 1 hr. 20 min. because patient moved at end of hour.
37.67	120	6.5	.97	18	8	74	1.57	46.61	
37.71	120	1.2	.98	18	6	76	1.57	46.44	
36.64									
36.62	99	1.2	.80	16	58	26	1.46	43.42	Basal.
36.80	100	9.2	.79	16	59	25	1.50	44.35	
37.07	105	4.0	.77	15	66	19	1.55	45.93	
35.49									
35.57	69	8.8	.84	18	44	38	1.13	33.63	Basal.
35.57	76	1.6	.83	18	49	33	1.15	34.43	
35.71	79	4.6	.78	17	57	26	1.23	36.74	

TABLE 5.—Clinical Calorimetry—

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Morris S.	Prelim.	11:45	.....	.....	..	.....	.....	.....	.....	.....	37.06
Jan. 27, '14 57.50 kg.	1	12:46	19.39	17.28	.82	21.44	0.365	67.63	69.67	56.44	36.79
	2	1:45	22.28	19.73	.82	21.96	0.365	65.98	71.20	73.22	36.90
	3	2:45	22.21	19.73	.82	22.74	0.365	65.94	70.02	72.00	36.97
Morris S.	Prelim.	11:27	.....	.....	..	.....	.....	.....	.....	.....	36.89
Dec. 17, '14 61.21 kg.	1	12:27	21.46	19.30	.81	25.58	0.381	64.27	70.65	64.61	36.70
	2	1:27	23.25	21.17	.80	27.85	0.381	70.42	72.99	70.69	36.79
	3	2:27	23.02	20.52	.82	27.74	0.381	68.53	72.30	68.84	36.81
Morris S.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	37.02
Dec. 18, '14 62.81 kg.	1	12:00	27.56	22.40	.90	31.97	0.409	76.31	77.07	71.53	36.92
	2	1:00	29.29	24.39	.87	34.09	1.101	81.43	84.04	82.67	36.94
	3	2:00	23.14	19.14	.88	29.33	1.101	63.50	76.85	73.79	36.89
	4	3:00	25.29	21.01	.88	31.79	1.101	69.82	78.61	74.47	36.85
Charles F.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	38.94
Nov. 10, '13 57.73 kg.	1	12:10	26.83	24.23	.81	26.28	0.514	80.56	66.11	79.70	39.21
	2	1:10	27.37	25.08	.79	28.78	0.514	83.17	71.87	73.83	39.26
	3	2:10	27.91	25.99	.78	43.30	0.614	85.95	88.09	77.90	39.06
Charles F.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	38.82
Nov. 11, '13 58.22 kg.	1	12:20	28.97	24.58	.86	25.84	0.930	82.03	67.32	78.06	39.05
	2	1:20	30.21	26.74	.82	31.12	0.930	88.58	77.70	86.98	39.25
	3	2:20	31.40	27.66	.83	31.13	0.930	91.78	82.04	99.99	39.63
Charles F. ...	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	39.62
Nov. 14, '13 57.94 kg.	1	12.10	32.69	26.60	.89	32.29	0.813	89.98	83.73	83.31	39.62
	2	1:10	31.92	25.64	.91	32.26	0.813	87.23	81.28	68.87	39.37
	3	2:10	32.24	26.33	.89	32.95	0.813	88.98	89.47	91.35	39.49
Charles F.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	39.77
Nov. 15, '13 57.03 kg.	1	12:16	28.26	26.44	.78	28.84	0.657	87.09	75.09	82.25	39.93
	2	1:16	28.23	26.08	.79	32.35	0.657	86.12	86.12	74.34	39.88
Charles F.	Prelim.	11:26	.....	.....	..	.....	.....	.....	.....	.....	36.71
Nov. 29, '13 50.36 kg.	1	12:26	21.39	18.31	.85	29.25	0.483	61.69	61.79	59.74	36.67
	2	1:26	22.05	20.15	.80	28.24	0.483	67.01	63.78	75.00	37.00
	3	2:26	21.99	19.44	.82	27.10	0.483	65.08	63.75	72.92	37.25
Charles F.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	36.90
Dec. 8, '13 50.99 kg.	1	12:10	25.97	19.63	.96	21.83	0.817	66.98	62.72	52.64	36.67
	2	1:10	26.73	21.61	.90	25.30	0.817	72.92	70.29	75.47	36.85
	3	2:10	25.97	21.12	.90	29.04	0.817	71.13	74.23	76.85	36.95
Charles F.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	36.78
Dec. 9, '13 50.38 kg.	1	12:06	22.60	18.05	.91	19.36	0.380	61.66	58.80	55.10	36.70
	2	1:06	22.10	17.29	.93	22.22	0.380	59.30	64.40	69.90	36.87
	3	2:06	21.98	17.63	.91	22.36	0.380	60.15	61.83	61.55	36.88
Charles F.	Prelim.	11:10	.....	.....	..	.....	.....	.....	.....	.....	36.89
Dec. 10, '13 51.09 kg.	1	12:10	26.98	20.24	.97	22.40	0.362	70.28	62.46	58.29	36.80
	2	1:10	27.70	19.45	1.04	24.37	0.362	68.24	68.32	64.48	36.76
	3	2:10	25.68	18.90	.99	28.76	0.362	65.28	72.63	60.44	36.50

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
85.61									
35.11	60	0.5	.82	17	51	32	1.00	31.29	Basal.
35.15	71	5.6	.82	15	51	34	1.15	35.82	
35.37	68	5.2	.82	15	52	33	1.15	35.80	
.....	62	4.0	.81	16	55	29	1.05	33.61	Basal.
.....	65	6.0	.80	14	58	28	1.15	36.83	
.....	62	5.0	.82	15	62	33	1.12	35.03	
.....	..	5.0	.91	14	21	65	1.22	39.23	At 8:40-9:40 a. m., protein meal; 9.6 gm. N.
.....	74	6.0	.92	36	17	47	1.30	41.87	
.....	70	6.0	.95	46	9	45	1.01	32.65	
.....	62	6.0	.93	42	14	44	1.11	35.90	
.....	76	8.5	.81	17	55	28	1.40	43.81	Basal.
.....	76	2.0	.79	16	60	24	1.44	45.23	
.....	82	9.0	.78	16	64	20	1.49	46.74	
37.69									
38.24	77	3.5	.88	30	28	42	1.41	44.34	9:10-10:10, protein meal; Nitrogen 6.6 gm.
38.25	88	13.0	.83	28	42	30	1.52	47.88	
38.34	84	4.0	.83	27	41	32	1.57	49.61	
38.79									
38.90	97	15.0	.93	24	19	57	1.56	48.80	At 10:21 a. m., 116 gm. commercial glucose.
38.68	98	8.3	.94	25	15	60	1.52	47.31	
38.79	96	25.0	.92	24	21	55	1.55	48.25	
38.92									
39.10	90	17.0	.77	20	63	17	1.53	47.75	Basal.
39.04	88	15.5	.78	20	59	21	1.51	47.22	
.....	80	13.2	.86	21	37	42	1.23	36.81	Basal.
.....	86(?)	16.5	.79	20	56	24	1.33	39.98	
.....	84	18.8	.83	20	47	33	1.30	38.83	
36.24									
36.54	74	36.6	1.05	32	..	68	1.31	39.54	9:03-9:45, protein meal; 10.5 gm. N. Work adder too high on account of rapid changes in barometer.
36.16	72	20.3	.94	30	13	57	1.43	43.05	
36.37	84(92)	15.0	.94	30	15	55	1.40	41.99	
....	75	22.3	.93	16	19	65	1.23	36.72	Basal.
.....	76	23.0	.96	17	12	71	1.18	35.32	
.....	84	9.7	.93	17	20	63	1.20	35.83	
.....	73	10.0	1.00	14	..	86	1.38	41.46	At 10:22, 115 gm. commercial glucose.
.....	87	23.5+2?	1.08	14	..	86	1.34	40.26	
.....	81	38.0+2?	1.02	15	..	85	1.29	38.81	

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Charles F. .... Dec. 26, '13 55.87 kg.	Prelim.	11:12	.....	.....	..	.....	.....	.....	.....	.....	36.84
	1	12:12	23.75	19.16	.90	26.72	0.275	65.56	75.47	75.27	36.90
	2	1:12	21.98	18.86	.85	25.23	0.275	63.65	69.83	67.08	36.86
	3	2:12	22.11	20.10	..80	25.14	0.275	67.03	70.63	69.23	36.85
Charles F. .... Dec. 31, '13 55.98 kg.	Prelim.	1:40	.....	.....	..	.....	.....	.....	.....	.....	37.06
	1	2:40	21.85	19.82	.80	22.56	0.403	65.85	66.09	59.70	36.95
	2	3:40	22.81	21.14	.78	26.98	0.403	69.98	69.09	68.75	36.95
Howard F. .... Nov. 7, '13 35.47 kg.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	39.74
	1	12:16	22.09	20.53	.78	22.79	.....	68.25	67.28	56.71	39.73
	2	1:16	21.02	19.75	.77	24.24	.....	65.53	64.17	63.90	39.73
	3	2 :16	20.86	.....	..	24.06	.....	65.03 ?	64.99	60.30	39.58
Howard F. .... Nov. 12, '13 34.98 kg.	Prelim.	11:24	.....	.....	..	.....	.....	.....	.....	.....	39.64
	1	12:24	22.06	19.37	.83	20.58	0.612	64.40	58.89	61.38	39.74
	2	1:24	23.23	20.40	.83	23.38	0.612	67.88	63.72	65.61	39.89
	3	2:24	22.55	21.27	.77	23.60	0.612	69.78	63.49	70.09	40.15
Howard F. .... Nov. 13, '13 34.19 kg.	Prelim.	11:00	.....	.....	..	.....	.....	.....	.....	.....	39.76
	1	12:00	19.45	17.76	.80	22.30	0.436	58.81	57.80	59.64	39.84
	2	1:00	19.64	18.48	.77	22.62	0.436	60.86	58.19	57.19	39.82
	3	2:00	20.20	19.24	.76	23.66	0.436	63.22	63.74	62.17	39.78
Howard F. .... Nov. 20, '13 32.54 kg.	Prelim.	11:30	.....	.....	..	.....	.....	.....	.....	.....	39.31
	1	12:30	18.43	17.26	.78	27.43	0.354	56.98	55.72	56.87	39.33
	2	1:30	18.27	17.42	.76	27.31	0.354	57.30	63.70	68.16	39.14
	3	2:30	17.96	17.42	.75	25.62	0.354	57.10	59.75	53.97	38.94
Howard F. .... Dec. 1, '13 32.93 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.03
	1	12:06	19.35	14.58	.97	18.80	0.292	50.50	45.34	42.26	36.93
	2	1:06	39.56	29.26	.98	37.03	0.292	101.68	46.88	97.14	36.96
	3	2:06							50.17		36.97
Howard F. .... Dec. 2, '13 33.06 kg.	Prelim.	11:12	.....	.....	..	.....	.....	.....	.....	.....	36.84
	1	12:12	16.46	12.42	.91	17.57	0.234	42.40	44.03	42.30	36.79
	2	1:12	18.09	13.48	.98	18.64	0.234	46.86	50.53	52.20	36.93
Howard F. .... Dec. 6, '13 34.74 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.07
	1	12:06	22.13	17.28	.93	21.01	0.614	58.85	55.03	51.80	36.97
	2	1:06	24.24	17.61	1.00	21.99	0.614	60.75	61.84	64.82	37.17
	3	2:06	24.72	19.43	.93	23.61	0.614	66.21	64.12	65.52	37.26
Howard F. .... Dec. 6, '13 33.78 kg.	Prelim.	10:56	.....	.....	..	.....	.....	.....	.....	.....	37.02
	1	11:56	18.20	13.44	.98	17.44	0.267	46.71	47.88	46.67	36.99
	2	12:56	19.17	14.84	.94	18.30	0.267	51.14	51.37	51.43	37.06
Howard F. .... Dec. 18, '13 37.17 kg.	Prelim.	11:06	.....	.....	..	.....	.....	.....	.....	.....	37.11
	1	12:06	19.11	16.10	.86	18.73	0.314	54.38	53.61	52.94	37.10
	2	1:06	21.42	18.19	.86	20.94	0.314	61.42	68.80	63.36	37.29
	3	2:06	20.93	18.62	.81	23.84	0.314	62.26	65.14	53.04	37.25

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
36.02									
36.09	76	28.2	.92	11	26	63	1.18	36.44	Basal
36.38	..	18.3	.85	11	44	45	1.14	35.38	
35.74	..	10.2	.80	11	61	28	1.20	37.26	
36.90									
35.98	78	4.0	.80	16	57	27	1.18	38.38	Basal.
36.68	81	....	.78	15	64	21	1.25	38.66	
.....	100	10.0	....	..	..	..	1.91	51.35	Basal. Urine not obtained; O_2 lost in third period.
.....	103	6.0	....	..	..	..	1.83	49.31	
.....	106	2.0	....	..	..	..	1.83(?)	48.93(?)	
39.01									
39.13	105	2.6	.84	25	41	34	1.84	48.90	9:10-9:40, protein meal; 6.5 gm. N. Asleep most of first period.
39.30	104	9.5	.84	24	42	34	1.94	51.65	
39.76	105	6.5	.76	23	63	14	2.00	52.99	
.....	108	1.0	.79	20	56	24	1.72	45.34	Basal.
.....	108	2.5	.77	19	65	16	1.78	46.92	
.....	104	7.7	.76	18	79	13	1.85	48.74	
39.14									
38.89	103	9.6	.77	16	65	19	1.75	45.41	Basal.
38.68	102	9.6	.75	16	70	14	1.76	45.66	
38.88	92	9.5	.74	16	75	9	1.75	45.50	
37.19									
37.16	98	2.6	1.00	15	1	84	1.53	39.92	At 10:19, 115 gm. commercial glucose; second and third periods averaged.
36.63	97	5.1	1.02	15	..	86	1.55	40.19	
37.21	97	6.0							
36.92									
36.83	75	2.5	.92	15	22	63	1.28	33.39	Basal. Asleep most of first hour.
36.60	76	15.6	1.01	13	..	87	1.42	36.90	
.....	91	7.0	.99	28	3	69	1.70	44.90	9.00-10:00, protein meal; 10.2 gm. N. Asleep first period.
.....	90	20.5	1.08	27	..	73	1.75	46.34	
.....	93	6.5(?)	.97	25	8	67	1.91	50.51	
.....	73	6.6	1.02	15	..	85	1.38	36.31	Basal. Asleep one-half first period.
.....	76	14.2	.96	14	11	75	1.51	39.75	
36.61									
36.82	104	5.5	.87	15	37	48	1.46	39.66	Basal. Asleep first period.
37.00	112	13.0	.87	14	40	46	1.65	44.79	
36.76	105	17.3	.82	13	53	34	1.68	45.40	

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Howard F. .... Dec. 30, '13 39.40 kg.	Prelim.	1:30	.....	.....	..	.....	.....	.....	.....	.....	37.29
	1	2:30	19.66	17.18	.83	22.45	0.278	57.68	62.50	55.92	37.10
	2	3:30	20.74	18.62	.81	23.93	0.278	62.21	60.31	61.45	37.17
Karl S. .... Jan. 5, '14 54.64 kg.	Prelim.	11:50	.....	.....	..	.....	.....	.....	.....	.....	40.14
	1	12:50	30.78	29.50	.76	39.97	0.720	96.73	101.70	91.12	39.92
	2	1:50	29.73	28.63	.76	42.23	0.720	93.48	104.45	93.93	39.70
Karl S. .... Jan. 6, '14 54.52 kg.	Prelim.	12:30	.....	.....	..	.....	.....	.....	.....	.....	39.53
	1	1:30	34.01	29.51	.84	26.77	0.879	98.46	87.72	112.04	40.08
	2	2:30	35.13	31.49	.81	34.31	0.879	104.43	104.39	99.22	40.05
	3	3:30	35.32	31.56	.81	38.70	0.879	104.75	107.68	105.06	40.02
Karl S. .... Jan. 16, '14 52.21 kg.	Prelim.	10:50	.....	.....	..	.....	.....	.....	.....	.....	38.29
	1	11:50	26.55	25.94	.74	26.51	0.786	84.44	.....	.....	38.32
	2	1:02	32.49	28.88	.82	38.71	0.943	95.01	.....	.....	38.22
	3	1:50	21.52	19.72	.80	32.34	0.655	64.72	.....	.....	38.14
Karl S. .... Jan. 19, '14 51.19 kg.	Prelim.	10:50	.....	.....	..	....	. ...	.....	.....	.....	36.36
	1	11:50	20.70	16.34	.92	12.72	0.522	55.62	.....	.....	36.54
	2	12:50	22.08	18.41	.87	28.28	0.522	62.03	.....	.....	36.55
	3	1:60	22.53	19.41	.84	32.55	0.522	64.98	.....	.....	36.57
Karl S. .... Jan. 21, '14 51.29 kg.	Prelim.	12:30	.....	.....	..	.....	.....	.....	.....	.....	36.72
	1	1:30	24.09	19.71	.89	32.46	6.858	66.11	.....	.....	36.55
	2	2:30	23.96	19.57	.89	25.79	0.858	65.65	.....	.....	36.39
	3	3:30	26.95	21.45	.91	32.17	0.858	72.55	.....	.....	36.46
Karl S. .... Jan. 22, '14 50.63 kg.	Prelim.	12:40	.....	.....	..	.....	.....	.....	.....	.....	36.75
	1	1:40	18.66	15.37	.88	16.87	0.428	51.92	.....	.....	36.54
	2	2:40	21.01	16.98	.90	20.51	0.428	57.70	.....	.....	36.46
	3	3:40	20.54	17.06	.88	22.17	0.428	67.62	.....	.....	36.48
Karl S. .... Feb. 6, '14 53.30 kg.	Prelim.	11:05	.....	.....	..	.....	.....	.....	.....	.....	37.15
	1	12:05	23.16	20.28	.83	23.98	0.324	68.07	67.32	58.11	36.95
	2	1:65	21.97	18.82	.85	22.85	0.324	63.43	67.46	56.97	36.72
	3	2:05	25.49	24.36	.76	27.16	0.324	80.44	74.45	80.28	36.86
Karl S. .... Feb. 7, '14 54.45 kg.	Prelim.	16:46	.....	.....	..	.....	.....	.....	.....	.....	37.35
	1	11:46	27.92	22.71	.89	32.41	0.581	77.05	77.13	60.51	36.99
	2	12:46	27.33	21.87	.91	29.12	0.581	74.43	79.33	74.46	36.89
	3	1:46	26.23	21.16	.90	32.41	0.581	71.85	79.75	76.71	36.83
Thomas B. .... Oct. 15, '13 73.62 kg.	Prelim.	10:48	.....	.....	..	.....	.....	.....	.....	.....	36.79
	1	11:48	24.87	22.60	.80	23.50	0.505	75.00	48.97	70.72	37.13
	2	12:48	27.05	22.82	.86	24.88	0.505	76.95	56.97	72.61	37.38
	3	1:48	26.46	24.69	.78	26.46	0.505	81.67	63.67	74.67	37.58
	4	2:48	28.39	24.58	.84	28.78	0.505	82.49	67.68	79.68	37.78
Thomas B. .... Oct. 21, '13 72.56 kg.	Prelim.	10:24	.....	.....	..	.....	.....	.....	.....	.....	36.69
	1	11:24	22.98	20.14	.83	24.71	0.407	67.43	.....	52.61	36.71
	2	12:24	24.90	19.11	.95	29.65	0.407	65.88	65.03	63.75	36.71
	3	1:24	26.13	20.21	.94	30.15	0.407	69.58	68.06	62.32	36.64

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
36.57									
36.44	109	6.6	.84	13	48	39	1.47	40.49	Basal. Asleep greater part of both periods.
36.60	107	8.5	.81	12	67	31	1.58	43.67	
39.24									
38.97	114	8.4	.75	20	69	11	1.77	54.93	Basal.
38.67	109	6.7	.75	20	69	11	1.71	53.08	
38.60									
39.61	107	8.8	.85	24	39	37	1.80	65.62	9:45-10:12, protein meal; 10.6 gm. N.
39.39	99(?)	14.6	.81	22	50	28	1.92	59.00	
39.27	119	13.0	.82	22	49	29	1.92	59.18	
.....	92	12.2	.72	25	70	5	1.62	49.09	Basal. Water ther. broken. Second period 72 min. long on account movement.
.....	96	21.0+3?	.82	26	44	30	1.53	46.03	
.....	96	11.0	.77	26	57	17	1.55	45.15	
.....	76	10.6	.96	25	9	66	1.09	32.74	Basal.
.....	76	14.8+4	.89	22	28	50	1.21	36.51	
.....	78	16.8	.86	21	39	40	1.27	38.25	
.....	73	9.8	.94	34	14	52	1.29	38.89	9:35-11:36, protein meal; 10.0 gm. N.
.....	69	5.7	.94	35	13	52	1.28	38.62	
.....	74	17.0	.97	31	7	62	1.42	42.68	
.....	69	4.0	.91	22	25	53	1.03	30.81	Basal. Asleep first period.
.....	57	11.7	.93	20	20	60	1.14	34.24	
.....	68	9.2	.90	20	29	51	1.14	34.20	
36.20									
36.52	81	15.5	.84	13	49	38	1.28	39.03	Basal. Asleep about 30 min. in first period and 50 min. in second.
35.86	79	9.4	.86	14	42	44	1.19	36.37	
35.97	82	25.2	.76	11	74	15	1.51	46.12	
36.40									
36.58	94	12.4	.92	20	22	58	1.41	43.56	7:30-7:40, 44.3 gm. protein; 9:35-9:37, 15.6 gm. protein; total, 9.6 gm. N. Asleep most of the time.
35.97	90	7.2	.94	21	16	63	1.37	42.07	
36.24	86	11.0	.93	21	19	60	1.32	40.62	
.....	81	8.0	.80	18	56	26	1.02	34.67	Basal.
.....	85	14.0	.88	17	35	48	1.05	35.58	
.....	84	7.6	.77	16	65	19	1.11	37.71	
.....	91	21.0	.85	16	43	41	1.12	38.14	
.....	73(?)	12.0	.84	16	47	37	0.93	31.48	Basal.
.....	78	19.0	.98	16	6	78	0.91	30.76	
.....	84	....	.97	16	9	75	0.96	32.48	

TABLE 5.—CLINICAL CALORIMETRY—

Subject Date Weight	Period	End of Period	Carbon-dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calorimetry, Cal.	Heat Eliminated, Cal.	Direct Calorimetry (Rectal Temp.) Cal.	Rectal Temp. C.
Richard T.	Prelim.	9:48	.....	.....	..	.....	.....	.....	.....	.....	38.13
Oct. 18, '13 36.49 kg.	1	10:48	20.39	18.59	.80	30.29	0.403	61.65	43.77	57.62	38.60
	2	11:48	21.05	18.24	.84	21.24	0.403	61.12	42.57	66.86	39.50
	3	12:48	20.49	18.68	.80	25.61	0.403	61.95 ?	45.94	52.35	39.74
Richard T.	Prelim.	10:16	.....	.....	..	.....	.....	.....	.....	.....	37.68
Oct. 20, '13 35.37 kg.	1	11:16	18.98	15.18	.91	31.21	0.499	51.48	42.37	58.44	38.24
	2	12:16	21.25	18.39	.84	31.41	0.499	61.49	47.46	58.51	38.63
	3	1:16	19.90	17.96	.81	29.74	0.499	59.49	48.42	46.90	38.64
Anton K.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	36.99
Oct. 16, '13 50.55 kg.	1	12:16	22.48	18.64	.88	30.88	0.479	62.98	61.00	61.00	36.99
	2	1:16	21.65	19.08	.83	33.40	0.479	63.64	66.45	72.34	37.14
	3	2:16	23.57	19.73	.87	30.29	0.479	66.57	64.84	68.64	37.24
Rose G.	Prelim.	11:04	.....	.....	..	.....	.....	.....	.....	.....	37.04
Nov. 22, '13 30.11 kg.	1	12:04	17.77	15.73	.82	28.24	.....	52.81	51.24	53.76	37.15
	2	12:34	9.28	7.28	.93	17.44	.....	24.98	28.36	24.99	37.02
Edw. B.	Prelim.	12:07	.....	.....	..	.....	.....	.....	.....	.....	38.07
Oct. 23, '14 55.76 kg.	1	1:07	25.02	22.61	.81	30.22	0.187	75.66	62.23	70.20	38.25
	2	2:07	25.51	23.48	.79	28.78	0.187	78.30	64.70	81.43	38.62
	3	3:07	27.24	25.59	.77	29.84	0.187	85.03	70.05	71.67	38.88
Edw. B.	Prelim.	11:24	.....	.....	..	.....	.....	.....	.....	.....	37.54
Oct. 26, '14 56.10 kg.	1	12:24	23.13	19.58	.86	31.21	0.264	66.36	61.58	66.23	37.65
	2	1:24	24.87	23.79	.76	29.49	0.264	78.72	60.08	67.98	37.83
	3	2:24	25.18	22.90	.80	30.36	0.264	76.47	65.45	73.34	38.01
	4	3:24	26.12	23.21	.82	31.13	0.264	77.87	70.55	84.46	38.32
Edw. B.	Prelim.	11:20	.....	.....	..	.....	.....	.....	.....	.....	37.40
Oct. 27, '14 56.84 kg.	1	12:20	24.80	21.91	.82	30.89	0.552	73.08	60.09	59.69	37.46
	2	1:20	23.76	22.13	.78	29.26	0.552	73.01	61.33	70.63	37.68
	3	2:20	23.24	22.30	.76	28.83	0.552	73.13	63.78	73.06	37.91
Edw. B.	Prelim.	11:15	.....	.....	..	.....	.....	.....	.....	.....	37.16
Nov. 4, '14 58.72 kg.	1	12:15	24.00	19.79	.88	31.79	0.337	67.32	64.06	64.69	37.18
	2	1:16	25.03	21.77	.84	31.06	0.337	73.17	65.16	69.21	37.27
	3	2:16	24.89	21.98	.82	31.62	0.337	73.72	70.13	74.19	37.36
Edw. B.	Prelim.	11:16	.....	.....	..	.....	.....	.....	.....	.....	38.84
Nov. 6, '14 59.78 kg.	1	12:16	26.21	23.22	.82	27.40	0.336	77.76	62.39	81.16	39.28
	2	1:15	26.65	23.45	.83	28.17	0.336	78.07	64.20	69.44	39.41
	3	2:15	26.61	23.39	.82	30.30	0.336	78.33	68.49	72.76	39.52
Edw. B.	Prelim.	11:15	.....	.....	..	.....	.....	.....	.....	.....	40.32
Nov. 10. '14 56.87 kg.	1	12:15	30.59	30.14	.74	35.32	0.525	98.74	88.56	86.50	40.33
	2	1:15	29.62	27.49	.78	36.30	0.526	90.99	87.53	91.26	40.43
	3	2:15	30.25	.....	..	39.54	0.525	.....	94.67	86.34	40.26
John K.	Prelim	11:56	.....	.....	..	.....	.....	.....	.....	.....	39.00
Dec. 15, '14 63.81 kg.	1	12:56	30.97	28.17	.80	34.02	1.258	92.29	85.30	94.23	39.26
	2	1:56	30.59	30.08	.74	39.95	1.258	97.14	91.58	87.82	39.22

—IN TYPHOID FEVER—(*Continued*)

Surface Temp., C.	Average Pulse	Work Adder., Cm.	Non-Protein, R. Q.	Per Cent. Calories from			Calories Per Hour		Remarks
				Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M.	
.....	81	31.4	.80	17	57	26	1.69	45.50	Basal. Somewhat restless.
.....	98	16.2	.85	17	43	40	1.68	45.11	
.....	..	18.5	.80	17	57	26	1.70	45.72	
.....	82	22.0	.95	26	13	61	1.45	38.79	Basal.
.....	102	30.0	.85	22	40	38	1.74	46.34	
.....	95	17.0	.81	22	50	28	1.68	44.83	
.....	76	21.0	.90	20	28	52	1.25	37.42	Basal.
.....	81	19.0	.83	20	46	34	1.26	37.81	
.....	80	13.0	.89	19	32	49	1.32	39.55	
35.75									
36.05	79	16.0	....	..	..	..	1.75	44.32	Basal. Restless. Second period ½ hr. long because patient voided in bed.
36.10	76	9.0	....	..	..	..	1.66	41.93	
.....	118	12.0	.81	7	49	44	1.36	42.10	Basal.
.....	115	17.0	.79	6	67	27	1.40	43.57	
.....	116	24.0	.77	6	73	21	1.53	47.32	
.....	105	11.0	.87	11	39	50	1.18	36.78	10:25 a. m., 79 gm. olive oil = 750 calories.
.....	117	10.0	.76	9	74	17	1.40	43.64	
.....	126	10.0	.80	9	62	29	1.36	42.39	
.....	123	15.0	.82	9	56	35	1.39	43.17	
.....	106	14.0	.83	19	47	34	1.29	40.16	Basal.
.....	109	22.0	.78	19	61	20	1.29	40.12	
.....	107	14.0	.75	19	69	12	1.29	40.18	
.....	102	10.6	.90	13	30	57	1.15	36.19	Basal.
.....	104	14.0	.84	12	48	40	1.25	39.34	
.....	106	25.0	.83	12	51	37	1.26	39.64	
.....	...	31.0	.82	11	54	35	1.30	41.32	Basal. Rising temp.
.....	124	5.0	.83	11	51	38	1.31	41.48	
.....	124	12.0	.82	11	54	35	1.31	41.62	
.....	141	24.0	.73	14	79	7	1.74	54.31	Basal. Very high temp. Mildly delirious.
.....	142	30.5	.78	15	64	21	1.60	50.05	
.....	140	16.0++							
.....	62	16.0	.80	36	43	21	1.45	46.94	Basal.
.....	63	14.0	.70	34	66	0	1.52	49.41	

TABLE 6.—CLINICAL DATA

CHARLES F.

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Nov. 6....	1,465	88.0	96.0	8.3	14.68	15.51†	—7.21	58.56	1,270
Nov. 7....	.....	.....	.....	....	16.62	.....	....	.....	1,600
Nov. 8....	1,856	116.0	123.0	9.1	21.10	22.01	—12.91	.....	2,300
Nov. 9....	2,065	130.0	135.0	10.8	20.45	21.53	—10.73	.....	1,870
Nov. 10....	1,088	80.0	69.0	4.4	16.22	16.66	—12.26	67.76	1,205
Nov. 11....	2,027	214.0	87.0	13.2	22.28	23.60	—10.40	58.25	1,740
Nov. 12....	2,610	251.0	144.0	9.8	18.92	19.90	—10.10	.....	2,110
Nov. 13....	2,265	218.0	118.0	10.2	17.37	18.39	—8.19	67.88	1,900
Nov. 14....	1,399	203.0	50.0	3.8	16.03	16.41	—12.61	67.60	1,235
Nov. 15....	1,286	148.0	60.0	4.6	18.54	19.00	—14.40	56.86	1,270
Nov. 16....	1,440	151.0	72.0	6.7	18.89	19.46	—13.76	.....	1,960
Nov. 17....	1,492	128.0	83.0	7.6	17.82	18.58	—10.98	.....	2,110
Nov. 18....	1,749	133.0	107.0	8.1	20.34	21.15	—13.05	56.01	1,470
Nov. 19....	1,019	63.0	68.0	5.2	22.13	22.65	—17.45	.....	1,360
Nov. 20....	1,328	93.0	76.0	8.7	22.41	23.28	—14.58	.....	1,380
Nov. 21....	1,426	74.0	98.0	8.1	22.81	23.62	—16.62	.....	1,380
Nov. 22....	1,970	122.0	128.0	10.9	20.50	21.59	—10.69	.....	1,900
Nov. 23....	1,787	112.0	115.0	10.6	18.16	19.22	—8.62	.....	1,680
Nov. 24....	1,696	117.0	101.0	10.4	18.16	19.20	—8.80	62.02	1,580
Nov. 25....	2,443	159.0	165.0	13.8	18.95	20.33	—6.53	.....	1,910
Nov. 26....	2,595	174.0	160.0	15.4	18.92	20.46	—5.06	51.48	20.50
Nov. 27....	2,345	173.0	142.0	12.3	18.41	19.64	—7.34	.....	1,920
Nov. 28....	2,646	223.0	150.0	13.1	16.65	17.96	—4.86	50.98	2,120
Nov. 29....	* 1,903	129.0	126.0	7.8	13.91	14.69	—6.89	50.29	1,150
Nov. 30....	2,825	236.0	158.0	15.2	15.58	17.10	—1.90	.....	1,700
Dec. 1....	3,491	314.0	195.0	14.9	14.12	15.61	—0.71	60.50	1,760
Dec. 2....	3,126	310.0	160.0	14.3	12.33	13.76	+0.54	.....	1,480+
Dec. 3....	2,595	279.0	118.0	13.7	11.99	13.36	+0.34	50.79	1,600
Dec. 4....	3,408	382.0	150.0	17.4	12.69	14.43	+2.96	.....	1,480
Dec. 5....	2,683	362.0	87.0	15.0	12.05	13.55	+1.45	.....	1,580
Dec. 6....	2,827	390.0	88.0	15.9	12.67	14.26	+1.64	49.83	1.401
Dec. 7....	3,223	446.0	106.0	16.0	12.72	14.32	+1.68	49.83	1,740
Dec. 8....	2,182	346.0	94.0	20.0	16.27	18.27	+1.73	51.02	1,220
Dec. 9....	2,426	308.0	91.0	12.5	12.04	13.29	—0.79	50.41	695
Dec. 10....	2.905	432.0	88.0	12.3	10.01	11.24	+1.06	50.80	1,100
Dec. 11....	3,486	503.0	107.0	16.7	9.47	11.14	+5.56	.....	1,640
Dec. 12....	3,768	556.0	115.0	16.3	9.92	11.55	+4.75	.....	1,500
Dec. 13....	4,025	619.0	129.0	18.2	10.48	12.30	+5.90	53.16	1,880
Dec. 14....	3,660	549.0	105.0	16.8	10.59	12.27	+4.53	.....	1,470

* Estimate heat production 1,725.

TABLE 6.—CLINICAL DATA—(*Continued*)

CHARLES F.—(*Continued*)

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Dec. 15....	4.032	585.0	124.0	18.8	9.93	11.81	+6.99	52.81	1,330+
Dec. 16....	3.921	573.0	118.0	18.6	11.67	13.53	+5.07	54.05	1,280
Dec. 17....	3,539	510.0	109.0	16.9	11.15	12.84	+4.06	.....	1,470
Dec. 18....	3,869	572.0	113.0	18.2	11.54	13.36	+4.84	.....	1,800
Dec. 19....	4,085	630.0	112.0	17.9	10.39	12.18	+5.72	.....	1,500
Dec. 20....	3,901	599.0	105.0	18.5	11.04	12.89	+5.61	.....	1,760
Dec. 21....	4.017	620.0	105.0	19.3	11.43	13.36	+5.94	.....	1,850
Dec. 22....	3,351	282.0	189.0	17.1	12.33	14.04	+3.06	55.43	1,700
Dec. 23....	3,722	241.0	249.0	16.4	11.46	13.10	+3.30	.....	1,180
Dec. 24....	3,739	228.0	254.0	17.5	13.14	14.89	+2.61	.....	1,440
Dec. 25....	.....	.....	.....	....	9.28	.....	....	.....	1.300
Dec. 26....	2,122	153.0	137.0	12.4	9.40	10.64	+1.76	55.91	1,940
Dec. 27....	3,636	254.0	224.0	20.0	12.16	14.16	+5.84	.....	1,600
Dec. 28....	3,614	247.0	226.0	19.4	12.86	14.80	+4.60	.....	1,640
Dec. 29....	3,818	221.0	259.0	19.0	12.78	14.66	+4.34	.....	1,820
Dec. 30....	4,899	256.0	347.0	24.2	11.49	13.91	+10.29	.....	1,480
Dec. 31....	2,131	202.0	103.0	13.3	11.53	12.86	+0.44	56.43	1,571
1914 Jan. 1....	3,949	347.0	161.0	18.6	11.54	13.40	+5.20	.....	1,000
Jan. 2....	3,587	287.0	202.0	22.0	8.10	10.30	+11.70	.....	860

† Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—Clinical Data—(*Continued*)

Morris S.

Date, 1913	Estimated Heat Production per 24 Hrs.	Food: Total Calories	Food: Carbohydrate, Gm.	Food: Fat, Gm.	Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Weight Kg.	Urine Volume, C.c.	Feces Fat
Oct. 23	.....	2,962	419.0	76.0	20.8	15.13	3.1*	18.2	+2.6	49.69	1,280	
Oct. 24	2,376	1,259	169.0	28.0	11.8	19.56	1.7*	21.3	—9.5	51.50	2,350	
Oct. 25	2,299	2,371	364.0	36.0	21.3	13.59	3.2*	16.8	+4.5	51.22	1,710	
Oct. 26	.....	4,375	471.0	101.0	19.5	20.34	2.9	23.2	—3.7	.....	3,000	
Oct. 27	.....	3,194	321.0	152.0	18.2	21.60	2.7	24.3	—6.1	51.26	2,170	
Oct. 28	2,200	2,332	242.0	116.0	10.0	17.43	1.5	18.9	—8.9	51.18	1,390	
Oct. 29	2,228	2,876	258.0	150.0	16.4	20.38	2.5	22.9	—6.5	50.17	1,465	
Oct. 30	.....	3,031	318.0	141.0	15.5	18.72	2.31	21.03	—5.5	49.85	1,580	9.74
Oct. 31	2,225	2,784	224.0	149.0	18.0	22.28	2.31	24.59	—6.6	50.32	1,830	9.74
Nov. 1	.....	3,089	327.0	147.0	14.8	17.48	2.31	19.79	—5.0	49.82	1,600	9.74
Nov. 2	.....	3,039	324.0	142.0	15.2	16.76	2.31	19.07	—3.9	.....	1,600	9.74
Nov. 3	2,205	3,039	324.0	142.0	15.2	17.39	2.31	19.70	—4.5	48.83	1,370	9.74
Nov. 4	.....	3,039	324.0	142.0	15.2	15.86	2.31	18.17	—3.0	49.63	1,220	9.74
Nov. 5	2,104	3,024	324.0	139.0	16.4	16.57	2.31	17.88	—2.6	48.48	1,160	9.74
Nov. 6	.....	3,039	325.0	147.0	15.4	13.51	2.3	15.8	—0.4	49.03	1,310	
Nov. 7	.....	3,034	327.0	140.0	15.0	12.39	2.3	14.7	+0.3	.....	1,220	
Nov. 8	.....	3,018	319.0	142.0	15.0	11.24	2.3	13.5	+1.5	48.73	1,310	
Nov. 9	.....	3,048	321.0	144.0	15.4	11.71	2.3	14.0	+1.4	.....	1,240	
Nov. 10	.....	2,969	305.0	144.0	14.9	12.05	2.2	14.3	+0.6	.....	2,000	
Nov. 11	.....	3,004	324.0	140.0	14.8	10.23	2.2	12.4	+2.4	48.05	1,220	
Nov. 12	.....	2,998	314.0	142.0	15.2	12.78	2.3	15.1	+0.1	.....	1,380	
Nov. 13	.....	2,998	314.0	142.0	15.2	11.43	2.3	13.7	+1.5	.....	1,480	
Nov. 14	....	3,181	331.0	142.0	15.4	10.54	2.3	12.8	+2.6	.....	1,390	
Nov. 16	.....	2,994	313.0	142.0	15.2	10.42	2.3	12.7	+2.6	.....	2,000	
Nov. 16	.....	3,134	341.0	144.0	15.3	11.44	2.3	13.7	+1.6	.....	1,820	
Nov. 17	1,876	3,076	333.0	142.0	15.2	13.32	2.3	15.6	—0.4	48.80	1,690	
Nov. 18	2,022	1,987	217.0	95.0	8.0	15.19	1.2	16.4	—8.4	49.06	1,440	
Nov. 19	.....	1,355	148.0	61.0	7.7	15.47	1.2	16.7	—9.0	.....	2,280	
Nov. 20	.....	1,727	199.0	79.0	7.0	15.13	1.1	16.2	—9.2	.....	1,300	
Nov. 21	.....	1,805	171.0	95.0	8.4	14.74	1.3	16.0	—7.6	.....	900	
Nov. 22	.....	2,292	153.0	152.0	10.1	14.85	1.5	16.4	—6.3	.....	800	
Nov. 23	.....	2,392	192.0	132.0	10.7	15.69	1.6	17.3	—6.6	.....	840	
Nov. 24	2,282	2,016	173.0	117.0	8.5	13.08	1.3	14.4	—5.9	46.98	890	
Nov. 25	2,301	2,298	187.0	123.0	15.1	13.66	2.3	16.0	—0.9	47.47	925	
Nov. 26	2,217	2,087	172.0	126.0	8.0	10.32	1.2	11.6	—3.6	45.84	780	
Nov. 27	.....	2,747	242.0	148.0	14.8	18.58	2.2	20.8	—6.0	.....	820	
Nov. 28	.....	2,741	256.0	140.0	15.0	12.44	2.3	14.7	+0.3	47.26	980	
Nov. 29	.....	3,033	324.0	142.0	15.0	11.82	2.3	14.1	+0.9	.....	1,370	
Nov. 30	.....	3,153	334.0	147.0	16.0	10.76	2.4	13.2	+2.8	.....	1,060	
Dec. 1	.....	3,091	333.0	142.0	15.7	9.81	2.4	12.2	+3.5	47.08	1,180	
Dec. 2	.....	3,090	340.0	142.0	15.3	9.69	2.3	12.0	+3.3	.....	1,660+	

* Feces analyzed October 30 to November 5. Feces nitrogen averaged 14.8 per cent. of food nitrogen. On all other days the feces nitrogen was calculated as 15 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)

MORRIS S.—(*Continued*)

Date, 1913	Estimated Heat Production per 24 Hrs.	Food			Food N., Gm.	Urine N., Gm.	Feces N., Gm.*	Excreta N., Gm.*	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Feces Fat
		Total Calories	Carbohydrate, Gm.	Fat, Gm.								
Dec 3	.....	3,189	356.0	141.0	16.0	8.52	2.4	10.9	+5.1	47.31	930	
Dec. 4	.....	3,118	250.0	180.0	16.0	8.70	2.4	11.1	+4.9	.....	1,500	
Dec. 5	.....	2,977	156.0	209.0	15.0	8.74	2.3	11.0	+4.0	.....	1,520	
Dec. 6	.....	2,998	161.0	209.0	15.0	9.76	2.3	12.1	+2.9	46.65	1,340	
Dec. 7	.....	3,297	202.0	221.0	16.0	9.08	2.4	11.5	+4.5	.....	1,640	
Dec. 8	.....	3,914	206.0	289.0	14.9	8.55	2.2	10.8	+4.1	.....	1.340	
Dec. 9	.....	3,989	219.0	290.0	15.2	7.65	2.3	10.0	+5.2	47.53	1,140	
Dec. 10	.....	3,989	219.0	290.0	15.2	8.85	2.3	11.2	+4.0	.....	1,650	
Dec. 11	.....	3,989	219.0	290.0	15.2	9.31	2.3	11.6	+3.6	48.46	1,850	
Dec. 12	1,857	3,552	222.0	226.0	21.3	9.87	3.2	13.1	+8.2	48.64	1,700	
Dec. 13	1,604	2,925	395.0	104.0	13.1	12.64	2.0	14.6	—1.5	48.10	1,935	
Dec. 14	.....	3,256	475.0	95.0	16.5	9.47	2.5	12.0	+4.5	.....	1,100	
Dec. 15	1,723	8,117	511.0	74.0	13.0	8.68	2.0	10.7	+2.3	47.87	1,229	
Dec. 16	1,703	2,132	275.0	76.0	11.6	10.24	1.7	11.9	—0.3	47.91	802	
Dec. 17	.....	3,985	440.0	193.0	15.5	9.30	2.3	11.6	+3.9	.....	1,240	
Dec. 18	.....	3,499	256.0	224.0	14.4	10.82	2.2	13.0	+1.4	.....	1,670	
Dec. 19	2,058	2,868	248.0	173.0	9.6	11.34	1.4	12.7	—3.1	48.34	1,282	
Dec. 20	2,081	2,748	150.0	190.0	14.1	13.41	2.1	15.5	—1.4	48.55	1,343	
Dec. 21	.....	3,426	204.0	232.0	16.0	17.32	2.4	19.7	—3.7	48.55	1,560	
Dec. 22	2,217	8,034	345.0	140.0	12.2	14.42	1.8	16.2	—4.0	48.50	1,223	
Dec. 23	1,982	2,499	121.0	186.0	10.7	11.94	1.6	13.5	—2.8	48.54	883	
Dec. 24	.....	3,357	206.0	225.0	16.5	13.06	2.5	15.6	+0.9	.....	1,480	
Dec. 25	.....	.....	.....	.....	....	10.90	...	....	.....	.....	1,200	
Dec. 26	.....	3,560	189.0	263.0	17.1	10.48	2.6	13.1	+4.0	49.70	1,680	
Dec. 27	.....	3,180	159.0	227.0	16.4	11.10	2.5	13.6	+2.8	.....	1,930	
Dec. 28	.....	3,128	157.0	224.0	15.6	11.43	2.3	13.7	+1.8	.....	1,740	
Dec. 29	.....	3,109	157.0	222.0	15.5	11.77	2.3	14.1	+1.4	.....	1,380	
Dec. 30	.....	3,277	170.0	235.0	15.5	11.72	2.3	14.0	+1.5	.....	1,710	
Dec. 31	.....	2,990	293.0	143.0	17.9	12.61	2.7	15.3	+2.6	.....	1,600	
1914 Jan. 1	.....	2,991	266.0	166.0	15.4	12.11	2.3	14.4	+1.0	.....	2,120	
Jan. 2	1,567	2,078	141.0	132.0	10.7	10.01	1.6	11.6	—0.9	49.22	1,340	
Jan. 3	.....	3,051	158.0	216.0	15.6	12.27	2.3	14.6	+1.0	.....	2,160	
Jan. 4	.....	3,070	162.0	216.0	15.7	10.40	2.4	12.8	+2.9	.....	1,730	
Jan. 5	.....	.....	.....	.....	....	11.21	...	....	.....	.....	1,580	
Jan. 6	.....	3,044	158.0	215.0	15.5	12.69	2.3	15.0	+0.5	.....	2,330	
Jan. 7	.....	3,045	158.0	215.0	15.5	11.66	2.3	14.0	+1.5	.....	1,800	
Jan. 8	.....	3,068	162.0	215.0	15.6	11.77	2.3	14.1	+1.5	.....	1,460	
Jan. 9	.....	3,063	162.0	215.0	15.6	11.66	2.3	14.0	+1.6	.....	1,660	
Jan. 10	.....	3,475	268.0	208.0	17.3	12.10	2.6	14.7	+2.6	.....	1,460	
Jan. 11	.....	3,739	354.0	191.0	19.8	12.22	3.0	15.2	+4.6	.....	1,560	
Jan. 12	.....	3,551	344.0	177.0	19.5	12.61	2.9	15.5	+4.0	.....	2,350	
Jan. 13	.....	4,198	382.0	222.0	22.1	11.49	3.3	14.8	+7.3	.....	1,520	

* Excreta nitrogen estimated as urine nitrogen + 15 per cent of food nitrogen.

TABLE 6.—Clinical Data—(*Continued*)

Howard F.

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.*	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Nov. 6....	1,264	83.0	81.0	6.7	12.83	13.50	—6.80	36.06	970
Nov. 7....	918	62.0	59.0	4.4	12.05	12.49	—8.09	35.74	640
Nov. 8....	1,538	87.0	107.0	7.0	12.75	13.45	—6.45	35.79	840
Nov. 9....	1,454	106.0	88.0	7.7	12.61	13.38	—5.68	.....	760
Nov. 10....	1,401	115.0	78.0	8.1	12.67	13.48	—5.38	.....	680
Nov. 11....	925	93.0	38.0	7.5	13.79	14.54	—7.04	34.60	750
Nov. 12....	950	98.0	40.0	7.3	13.42	14.15	—6.85	35.01	830
Nov. 13....	1,260	134.0	60.0	5.8	12.52	13.10	—7.30	34.22	610
Nov. 14....	580	52.0	30.0	3.4	10.42	10.76	—7.36	.....	500
Nov. 15....	1,152	83.0	69.0	6.6	11.10	11.76	—5.16	33.36	900
Nov. 16....	1.096	150.0	40.0	4.4	9.98	10.42	—6.02	.....	500
Nov. 17....	1,462	123.0	83.0	7.2	9.30	10.02	—2.82	33.12	400
Nov. 18....	1,588	128.0	91.0	8.5	10.20	11.05	—2.55	32.93	590
Nov. 19....	984	63.0	62.0	6.7	10.65	11.22	—6.52	.....	780
Nov. 20....	1,288	74.0	75.0	7.3	10.25	10.98	—3.68	32.57	550
Nov. 21....	1,466	91.0	95.0	8.1	11.32	12.13	—4.03	.....	700
Nov. 22....	1,198	73.0	94.0	8.8	11.12	12.00	—3.20	.....	800
Nov. 23....	1,789	92.0	121.0	11.6	11.16	12.31	—0.71	.....	660
Nov. 24....	1,846	146.0	145.0	10.6	10.82	11.88	—1.28	.....	820
Nov. 25....	2,060	138.0	129.0	11.4	9.81	10.95	+0.45	32.14	940
Nov. 26....	2,686	176.0	168.0	15.7	10.42	11.99	+3.71	.....	780
Nov. 27....	2,240	211.0	118.0	10.9	9.47	10.56	+0.34	.....	570
Nov. 28....	2,742	245.0	145.0	15.0	9.98	11.48	+3.52	32.25	920
Nov. 29....	2,581	211.0	152.0	11.9	8.52	9.71	+2.19	.....	620
Nov. 30....	2,922	273.0	163.0	14.8	9.53	11.01	+3.79	.....	1,220
Dec. 1....	2,581	309.0	112.0	10.6	7.77	8.83	+1.77	.....	870
Dec. 2....	2,298	247.0	110.0	10.0	7.69	8.69	+1.31	33.09	900
Dec. 3....	3,689	423.0	163.0	17.2	9.25	10.97	+6.23	.....	900
Dec. 4....	3,627	441.0	147.0	17.7	9.00	10.77	+6.93	.....	1.130
Dec. 5....	2,671	337.0	81.0	21.0	13.01	15.11	+5.89	34.77	1,500
Dec. 6....	2,476	333.0	83.0	12.9	9.20	10.49	+2.41	33.81	775
Dec. 7....	3,621	496.0	119.0	19.0	10.45	12.35	+6.65	.....	1,500
Dec. 8....	3,391	434.0	112.0	17.8	9.89	11.67	+6.13	.....	1,270+
Dec. 9....	3,042	386.0	108.0	18.0	10.73	12.53	+5.47	36.51	1,300
Dec. 10....	2,986	394.0	101.0	16.8	10.51	12.19	+4.61	.....	1.450
Dec. 11....	3,149	405.0	114.0	17.8	10.79	12.57	+5.23	35.99	1,450
Dec 12....	3,100	417.0	101.0	17.5	10.36	12.11	+5.39	.....	1,610
Dec. 13....	3,644	472.0	122.0	18.5	10.03	11.88	+6.62	36.66	1,280

TABLE 6.—Clinical Data—(*Continued*)

Howard F.—(*Continued*)

Date, 1913	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.*	Body Wt., Kg.	Urine Vol., C.c.
	Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Dec. 14....	3,338	402.0	133.0	17.8	11.01	12.79	+5.01	.....	1,880
Dec. 15....	3,280	510.0	130.0	19.2	12.98	14.90	+4.30	37.54	1,890+
Dec. 16....	3,511	444.0	129.0	19.2	13.28	15.20	+4.00	.....	1,580
Dec. 17....	3,170	345.0	139.0	18.0	9.95	11.75	+6.25	39.10	1,720
Dec. 18....	2,008	248.0	78.0	10.5	8.57	9.62	+0.88	37.17	1,600
Dec. 19....	3,550	411.0	144.0	20.3	11.89	13.92	+6.38	.....	2.050
Dec. 20....	2,671	110.0	197.0	15.0	8.10	9.60	+5.40	.....	1,540
Dec. 21....	2,383	104.0	175.0	12.6	10.65	11.91	+0.69	.....	1,250
Dec. 22....	2,936	159.0	198.0	17.3	13.23	14.96	+2.34	37.21	1,150
Dec. 23....	3,520	239.0	235.0	13.9	9.19	10.58	+3.32	.....	1,200
Dec 24....	3,605	219.0	243.0	17.4	10.70	12.44	+4.96	.....	1,700
Dec. 25....	.....	.....	.....	....	10.42	.....	......	.....	1,370
Dec. 26....	3,152	219.0	199.0	15.6	9.77	11.33	+4.27	39.46	2,100
Dec. 27....	3,303	257.0	196.0	16.8	10.03	11.71	+5.09	.....	1.600
Dec. 28....	2,946	200.0	186.0	15.4	7.51	9.05	+6.35	.....	1.080
Dec. 29....	4,199	265.0	278.0	20.5	10.87	12.92	+7.58	.....	1,640
Dec. 30....	2,325	165.0	145.0	11.4	7.81	8.95	+2.45	39.39	987
Dec. 31....	3,569	317.0	192.0	18.5	11.77	13.62	+4.88	.....	1,500
1914 Jan. 1....	2,912	236.0	169.0	14.5	9.02	10.47	+4.03	.....	1,600
Jan. 2....	2,891	224.0	156.0	16.0	8.74	10.34	+5.66	.....	1,540

* Excreta nitrogen estimated as urine nitrogen + 10 per cent of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)

KARL S.

Date, 1914	Estimated Heat Production per 24 Hrs.	Food			Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.*	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.
		Total Calories	Carbohydrate, Gm.	Fat, Gm							
Jan. 3	.....	2,038	104.0	145.0	10.8	20.62	...	21.60	—10.80	.....	880
Jan. 4	.....	1,301	113.0	71.0	5.9	21.72	...	22.41	—15.61	.....	1,240
Jan. 5	2,579	1,119	95.0	54.0	5.4	.....	...	.....	......	64.67	726
Jan. 6	2,707	1,332	167.0	32.0	13.6	22.36	...	23.72	—10.12	64.31	1,010
Jan. 7	.....	1,942	93.2	136.0	11.3	.....	...	.....	......	.....	810
Jan. 8	.....	2,331	136.0	156.0	12.5	16.03	...	17.28	—4.78	.....	860
Jan. 9	.....	1,892	114.0	126.0	9.8	23.84	...	24.82	—15.02	62.99	1,700
Jan. 10	.....	2,910	223.0	174.0	14.6						
Jan. 11	.....	3,018	318.0	139.0	16.4						
Jan. 12	.....	3,017	322.0	138.0	16.2	18.15	1.6	19.8	—3.6	.....	2,310
Jan. 13	.....	2,966	326.0	128.0	17.2	13.94	1.7	15.6	+1.6	.....	1,820
Jan. 14	.....	2,802	313.0	118.0	16.4	17.06	1.6	18.7	—2.3	.....	1,830
Jan. 15	.....	3,129	323.0	149.0	16.2	18.65	1.6	20.3	—4.1	62.74	1,920
Jan. 16	2,208	2,448	226.0	132.0	11.5	19.11	1.2	20.3	—8.8	52.24	1,960
Jan. 17	.....	3,398	340.0	166.0	17.9	19.15	1.8	21.0	—3.1	.....	1,940
Jan. 18	.....	3,188	329.0	145.0	17.1	17.26	1.7	19.0	—1.9	.....	1,920
Jan. 19	1,661	2,795	268.0	145.0	13.6	14.72	1.4	16.1	—2.5	51.21	1,260
Jan. 20	.....	2,965	313.0	138.0	15.7	14.61	1.6	16.1	—0.4	.....	1,550
Jan. 21	1,798	2,912	315.0	129.0	16.3	17.57	1.6	19.2	—2.9	51.52	1,870
Jan. 22	1,512	2,605	253.0	133.0	12.8	13.25	1.3	14.5	—1.8	51.18	1,194
Jan. 23	.....	3,033	324.0	140.0	15.9	11.99	1.6	13.6	+2.3	.....	1,360
Jan. 24	.....	2,982	316.0	138.0	15.8	13.06	1.6	14.7	+1.1	.....	1,960
Jan. 25	.....	2,987	316.0	139.0	15.8	13.17	1.6	14.8	+1.0	.....	1,400
Jan. 26	.....	3,641	408.0	155.0	16.7	12.64	1.7	14.3	+2.4	54.64	1,620
Jan. 27	.....	3,999	439.0	191.0	16.3	13.06	1.6	14.7	+1.6	.....	1,460
Jan. 28	.....	4,025	439.0	194.0	16.3	11.88	1.6	13.5	+2.8	.....	1,280
Jan. 29	.....	3,975	438.0	190.0	16.1	11.32	1.6	12.9	+3.2	52.64	1,450
Jan. 30	.....	3,991	439.0	191.0	16.2	10.65	1.6	12.3	+3.9	.....	1,500
Jan. 31	.....	3,922	418.0	193.0	16.2	10.93	1.6	12.5	+3.7	.....	1,400
Feb. 1	.....	3,940	418.0	194.0	16.3	10.63	1.6	12.2	+4.1	.....	1,500
Feb. 2	.....	3,808	419.0	180.0	16.0	11.21	1.6	12.8	+3.2	.....	1,910
Feb. 3	.....	3,808	419.0	180.0	16.0	11.15	1.6	12.8	+3.2	.....	1,980
Feb. 4	.....	3,971	442.0	188.0	16.0	10.87	1.5	12.5	+3.5	.....	1,870
Feb. 5	.....	3,974	438.0	191.0	16.0	9.29	1.6	10.9	+5.1	.....	1,640
Feb. 6	1,916	3,232	330.0	165.0	13.3	10.24	1.3	11.6	+1.8	53.33	1,360
Feb. 7	1,965	3,526	387.0	148.0	22.1	.....	2.2	17.3	+4.8	54.48	2,300
Feb. 8	.....	4,018	474.0	178.0	16.3	11.67	1.6	13.3	+3.0	.....	1,440

* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

6.—Clinical Data—(*Continued*)

Thomas B.

Date 1913	Temperature		Food			Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Feces Fat
	Max.	Min.	Total Calories	Carbo-hy-drate, Gm.	Fat, Gm.								
Oct. 7	103.0	101.4	3,052	168.0	212.0	15.0	24.55	2.09	26.64	—11.64	76.08	1,240	9.19
Oct. 8	103.6	101.2	3,010	163.0	210.0	15.0	25.50	2.09	27.59	—12.59	75.61	1,270	9.19
Oct. 9	104.0	101.6	3,010	163.0	210.0	15.0	21.29	2.09	23.38	—8.38	75.73	1,120	9.19
Oct. 10	103.6	101.6	3.030	163.0	212.0	15.0	23.67	2.09	25.76	—10.76	76.02	1,740	9.19
Oct. 11	103.0	101.0	3.014	479.0	71.0	14.9	20.12	1.89	22.01	—7.11	74.85	1,500	5.80
Oct. 12	102.8	101.6	3,018	480.0	71.0	15.0	17.77	1.89	19.66	—4.66	.....	1,960	5.80
Oct. 13	102.4	100.6	3,014	479.0	71.0	14.9	18.77	1.89	20.66	—5.76	74.24	1,980	5.80
Oct. 14	103.0	100.0	3.045	173.0	212.0	14.2	18.21	1.28	19.49	—5.29	74.38	1,220	6.02
Oct. 15	102.2	98.6	2,670	130.0	187.0	11.7	18.61	1.28	19.89	—8.19	.....	1,040	5.02
Oct. 16	101.0	99.4	3,058	168.0	212.0	15.4	21.04	1,28	22.32	—6.92	.....	1,010	5.02
Oct. 17	101.6	99.4	3,211	484.0	78.0	15.6	17.79	....	19.35*	—3.75	73.10	1,120	
Oct. 18	100.6	99.0	2,998	476.0	71.0	15.0	15.69	....	17.19	—2.19	.....	1,100	
Oct. 19	99.6	98.6	3,019	481.0	71.0	16.0	15.30	....	16.80	—1.80	.....	1,220	
Oct. 20	99.6	98.6	3,002	468.0	75.0	15.0	15.24	....	16.74	—1.74	72.82	1,880	
Oct. 21	98.6	99.4	2,675	412.0	68.0	13.0	15.75†	....	.....	....	.....	1,610+	(?)
Oct. 22	99.6	98.8	2,943	462.0	71.0	15.0	16.32	....	17.82	—2.82	.....	1,480	
Oct. 23	99.6	98.6	3,062	449.0	76.0	21.2	16.76	....	18.88	+2.32	.....	1,230	
Oct. 24	99.6	98.6	3,396	541.0	60.0	20.0	13.34	....	15.34	+4.66	72.88	1,640	
Oct. 25	99.6	98.6	3,211	493.0	71.0	20.0	16.59	....	18.59	+1.41	.....	1,120	
Oct. 26	99.0	98.2	3,066	164.0	215.0	15.6	18.90	....	20.45	—4.95	.....	1,320	
Oct. 27	99.6	98.4	3,159	164.0	219.0	17.5	17.65	....	19.40	—1.90	.....	2,280	
Oct. 28	99.0	98.2	3,277	182.0	220.0	18.5	14.18	....	16.03	+2.47	73.69	1,220	

† This is the total for 19¾ hours.
* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—Clinical Data—(*Continued*)

Richard T.

Date 1913	Temperature		Food			Food N., Gm.	Urine N., Gm.	Feces N., Gm.	Excreta N., Gm.	Nitrogen Balance, Gm.	Body Weight, Kg.	Urine Volume, C.c.	Feces Fat
	Max.	Min.	Total Calories	Carbo-hy-drate, Gm.	Fat, Gm.								
Oct. 17	103.6	101.4	1.656	248.0	38.0	11.3	13.95	0.84	14.79	—3.49	36.09	2,290	1.63
Oct. 18	104.2	100.8	1,143	115.0	49.0	8.4	12.48	0.84	13.32	—4.92	.....	1,145	1.63
Oct. 19	103.2	100.8	2,131	327.0	49.0	13.0	14.40	0.84	15.24	—2.24	.....	1,720	1.63
Oct. 20	104.0	100.0	2,020	280.0	55.0	14.0	14.53	0.84	15.37	—1.37	.....	1,005	1.63
Oct. 21	102.8	100.0	2,359	360.0	51.0	16.0	15.13	0.84	15.97	+0.03	.....	1,320	1.63
Oct. 22	102.4	99.4	2,092	315.0	46.0	14.7	14.74	0.84	15.58	—0.88	35.57	1,200	1.63
Oct. 23	103.0	99.0	2,576	369.0	67.0	17.4	16.30	0.84	17.14	+0.26	35.70	1,570	1.63
Oct. 24	102.0	99.4	2,153	333.0	35.0	18.0	15.69	0.84	16.53	+1.47	.....	1,340	1.63
Oct. 25	101.0	98.4	2,519	228.0	125.0	16.0	16.32	0.84	17.16	—1.16	.....	1,260	1.63
Oct. 26	100.6	99.0	2,093	115.0	133.0	15.0	16.53	....	* 18.03	—3.03	.....	1,100	
Oct. 27	100.2	98.6	2,163	121.0	136.0	15.7	16.34	....	17.91	—2.21	35.30	1,200	
Oct. 28	99.6	98.6	2,009	124.0	117.0	16.0	16.47	....	18.07	—2.07	35.60	1,460	
Oct. 29	100.0	98.6	3,276	348.0	157.0	15.2	14.01	....	15.53	—0.33	.....	1,370	
Oct. 30	100.0	99.0	2,969	302.0	144.0	15.1	11.77	....	13.28	+1.82	35.38	1,195	
Oct. 31	101.6	99.2	2,954	310.0	142.0	15.5	12.05	....	13.60	+1.90	.....	1,420	
Nov. 1	102.0	100.4	3,069	334.0	142.0	14.5	11.32	....	12.77	+1.73	36.08	1,320	
Nov. 2	102.4	99.6	2,995	325.0	138.0	14.5	11.74	....	13.19	+1.31	.....	1,900	
Nov. 3	101.0	99.6	2,984	316.0	140.0	15.1	11.99	....	13.50	+1.60	36.27	1,270	
Nov. 4	100.2	99.4	3,037	320.0	144.0	15.2	12.22	....	13.74	+1.46	36.42	1,560	

* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)
EDWARD B.

Date, 1914	Estimated Heat Production per 24 Hrs.	Food			Food N., Gm.	Urine N., Gm.	Excreta N., Gm.*	Nitrogen Balance Gm.	Body Weight, Kg.	Urine Volume, C.c.
		Total Calories	Carbohydrate, Gm.	Fat, Gm.						
Oct. 14	.....	3,901	214.9	284.8	14.5	14.51	15.96	—1.46	56.29	1,180
Oct. 15	.....	4,171	212.9	309.3	16.4	11.39	13.03	+3.4	.....	1.415
Oct. 16	.....	4,003	662.0	97.2	15.0	11.49	12.99	+2.0	56.36	1,665(?)
Oct. 17	.....	1,561	236.3	43.8	7.28	8.65	9.37	—2.09	56.94	1,140
Oct. 18	.....	2,976	94.5	236.9	15.0	11.08	12.68	—2.42	56.01	1,690
Oct. 19	.....	4,217	111.0	362.1	13.9	16.17	17.56	—3.66	56.98	2,230
Oct. 20	.....	4,097	114.9	348.9	14.80	10.96	12.44	+2.36	56.67	1.520
Oct. 21	.....	3,586	518.9	114.7	15.20	9.17	10.69	+4.51	57.21	1,250
Oct. 22	.....	3,076	579.6	54.2	7.68	7.85	8.61	—0.93	56.60	1,170
Oct. 23	2,160	3,462	152.8	269.1	12.90	8.21	9.50	+3.40	55.76	835
Oct. 24	.....	4,072	220.6	299.4	15.0	11.94	13.44	+1.56	56.84	1,465
Oct. 25	.....	4,114	220.9	303.1	15.1	11.20	12.70	+2.40	66.73	1,515
Oct. 26	1,976	2,704	151.4	124.1	6.9	6.75	7.44	—0.54	.....	663
Oct. 27	1,982	3,844	109.1	334.5	11.1	8.61	9.72	+1.38	.....	1,125
Oct. 28	.....	4,056	223.4	295.7	15.2	8.19	9.71	+5.49	57.51	2,155
Oct. 29	.....	4,185	314.8	265.7	16.5	8.70	10.35	+6.15	57.46	1,960
Oct. 30	.....	3,643	364.7	179.0	18.8	10.30	12.18	+6.62	57.83	2.310
Oct 31	.....	3,893	402.5	191.4	18.0	9.72	11.52	+6.48	.....	1.655
Nov. 1	.....	4,394	455.7	218.4	19.3	11.05	12.98	+6.32	58.53	2,450
Nov. 2	.....	4,491	451.6	225.8	21.0	11.80	13.9	+7.1	58.76	1,770
Nov. 3	.....	4,836	491.9	244.6	21.2	12.20	14.32	+6.88	59.52	2,405
Nov. 4	1,936	2,209	209.4	119.7	9.2	9.20	10.12	—0.92	.....	979
Nov. 5	.....	3,960	390.5	195.9	17.0	10.59	12.29	+5.71	.....	1,665
Nov. 6	2,117	1,907	219.5	85.9	8.0	10.96	11.76	—3.76	.....	1,523
Nov. 7	.....	1,006	101.2	49.8	5.05	12.13	12.63	—7.58	59.23	1.075
Nov. 8	.....	398	64.0	11.8	1.08	10.34	10.44	—9.36	.....	665
Nov. 9	.....	617	94.8	20.0	1.68	11.26	11.42	—9.74	57.06	645
Nov. 10	2,632	1,103	104.3	51.2	6.0	14.72	15.32	—9.32	.....	833
Nov. 11	.....	1,646	96.0	84.2	9.7	16.73	17.70	—8.0	57.11	1,230
Nov. 12	.....	2,196	165.9	119.3	10.7	14.79	15.8	—5.1	.....	1,250

* Excreta nitrogen estimated as urine nitrogen + 10 per cent. of food nitrogen.

TABLE 6.—CLINICAL DATA—(*Continued*)
JOHN K.

Date, 1913	Total Calories	Carbohydrate, Gm.	Fat, Gm.	Food N., Gm.	Urine N., Gm.	Excreta N., Gm.	Nitrogen Bal., Gm.	Body Wt., Kg.	Urine Vol., C.c.
Dec. 15....	* 2,194	139.1	148.9	9.3	24.58	25.51	—16.21	63.81	1,152
Dec. 16....	3,309	145.1	246.8	16.3	21.45	23.08	—6.78	63.55	1,180
Dec. 17....	3,521	181.9	258.1	14.6	22.37	23.83	—9.23	63.27	3,110
Dec. 18....	3,205	181.9	223.6	14.8	19.30	20.78	—5.98	63.35	3,040
Dec. 19....	3,788	251.6	249.6	17.0	19.40	21.10	—4.10	63.05	3,230
Dec. 20....	3,916	259.7	257.1	18.0	18.26	20.06	—2.06	62.37	3,460
Dec. 21....	4,134	342.5	238.4	20.0	19.33	21.33	—1.33	63.04	4,285
Dec. 22....	4,658	378.4	267.2	20.4	18.00	20.04	+0.36	62.64	4,255
Dec. 23....	4,838	393.9	285.8	22.0	17.93	22.13	—0.13	63.26	3,210
Dec. 24....	4,450	373.1	259.1	19.9	18.78	20.77	—0.87	63.32	3,350

* Estimated heat production, 2,568 calories.

TABLE 7.—SUMMARY OF CLINICAL CALORIMETRY IN TYPHOID FEVER

Subject and Date	Character of Experiment	Period of Disease	Average Rectal Temp. C.	Average Pulse Rate	Average Respiratory Quotient	Indirect Calorimetry Average per Hour: Cal. per Kg.	Indirect Calorimetry Average per Hour: Cal. per Sq. M.	Per Cent. Divergence of Direct Cal. from Indirect Calories: According to Rectal Temp.	Per Cent. Divergence of Direct Cal. from Indirect Calories: According to Surface Temp.	Per Cent. Rise Above Normal Aver. Basal of 34.7 Cal. per Sq. M.	Per Cent. Rise Above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison
Morris S. 25	9.0 gm. N.........	Continued temperature	40.0	99	.77	1.70	51.42	— 5	......	+48		
Oct. 24, 1913	Basal.............	Continued temperature	39.5	101	.84	1.70	51.27	— 2	......	....	— 0.3	Oct. 24.
28	115.0 gm. glucose..	Continued temperature	39.2	111	.93	1.64	49.35	+ 1	......	....	+ 0.6	Oct. 29.
29	Basal.............	Continued temperature	39.6	106	.79	1.62	49.04	— 1	......	+41		
31	10.3 gm. N.........	Early steep curve.......	39.1	100	.84	1.68	50.24	—11	......	....	+ 2.4	Oct. 29.
Nov. 3	Restless..........	Early steep curve.......	38.9	108	.80	1.66	49.46	— 9	......	+43		
5	Basal.............	Early steep curve.......	38.1	106	.81	1.60	47.31	— 4	......	+36		
17	Basal.............	First Relapse Ascending temperature	38.7	108	.81	1.44	42.52	— 1	+ 1	+23		
18	Basal.............	Ascending temperature	39.9	118	.83	1.53	45.38	+ 1	— 1	+31		
24	Basal.............	Continued temperature	39.4	124	.76	1.79	52.69	—17	......	+52		
25	8.7 gm. N.........	Continued temperature	39.2	118	.81	1.84	54.17	— 8	......	....	+ 3.9	Av. Nov. 24 and 26.
26	Basal.............	Early steep curve.......	39.1	118	.76	1.78	51.60	—17	......	+49		
Dec. 12	10.6 gm. N.........	7th day, normal temp.	37.0	94	.84	1.45	42.89	— 9	— 8	....	+18.1	Dec. 13.
13	Basal.............	8th day, normal temp.	37.0	83	.82	1.23	36.33	+ 0	+ 4	+ 5		
15	115 gm. glucose....	10th day, normal temp.	37.2	95	1.01	1.36	40.07	— 8	—11	....	+ 3.7	Dec. 16.
16	Basal.............	11th day, normal temp.	37.3	88	.88	1.31	38.67	— 2	+ 0	+11		
19	115 gm. glucose....	Second Relapse Ascending temperature	39.4	116	.93	1.60	47.46	+ 2	— 4	....	+ 1.3	Dec. 20.
20	Basal.............	Early steep curve.......	39.6	113	.78	1.61	46.83	— 1	— 2	+35		
22	115 gm. glucose....	Early steep curve.......	39.2	116	.94	1.55	46.04	+11	+10	....	+ 0.7	Av. Dec. 20 and 26.
23	Basal.............	Early steep curve.......	38.3	101	.79	1.50	44.57	+ 5	+ 2	+28		
Jan. 2, 1914	Basal.............	8th day, normal temp.	37.0	75	.81	1.17	34.93	+ 3	+ 5	+ 1		
27	Basal.............	33d day, normal temp.	36.9	66	.82	1.10	34.30	+ 7	+ 4	—1		
Dec. 17, 1914	Basal.............	One year later.........	36.8	63	.81	1.10	35.16	+ 0	......	+ 1		
18	9.6 gm. N.........	One year later.........	36.9	68	.88	1.16	37.44	+ 4	......	....	+ 6.5	Dec. 17, 1914.

TABLE 7.—SUMMARY OF CLINICAL CALORIMETRY IN TYPHOID FEVER—(*Continued*)

Subject and Date	Character of Experiment	Period of Disease	Average Rectal Temp. C.	Average Pulse Rate	Average Respiratory Quotient	Indirect Calorimetry Average per Hour		Per Cent. Divergence of Direct Cal. from Indirect Calories		Per Cent. Rise Above Normal Aver. Basal of 34.7 Cal. per Sq. M.	Per Cent. Rise Above Patient's Own Basal Metabolism	Day of Basal Determination Used for Comparison
						Cal. per Kg.	Cal. per Sq. M.	According to Rectal Temp.	According to Surface Temp.			
Charles F. Nov. 10, 1913	Basal............	Ascending temperature	39.1	78	.79	1.44	45.26	— 7	— 6	+30		
11	6.6 gm. N.........	Ascending temperature	39.2	82	.84	1.50	47.28	+ 1	— 2	....	+ 4.5	Nov. 10, 1913.
14	115 gm. glucose....	Continued temperature	39.5	97	.90	1.54	48.12	— 8	— 6	....	+ 1.3	Nov. 15.
15	Basal............	Continued temperature	39.9	89	.78	1.52	47.49	—10	— 9	+37		
29	Basal............	Early steep curve.......	36.9	83	.82	1.29	38.54	+ 2	......	+11		
Dec. 8	10.5 gm. N........	7th day, normal temp.	36.8	77	.92	1.38	41.53	— 3	......	....	+15.5	Dec. 9.
9	Basal............	8th day, normal temp.	36.8	78	.92	1.20	35.96	+ 3	......	+ 4		
10	115 gm. glucose....	9th day, normal temp.	36.7	80	1.00	1.33	40.18	—10	......	....	+11.7	Dec. 9.
26	Basal...........	25th day, normal temp.	36.9	76	.85	1.17	36.86	+ 8	+ 1	+ 5		
31	Basal............	30th day, normal temp.	37.0	80	.79	1.21	37.52	— 5	— 6	+ 8		
Howard F. Nov. 7, 1914	Basal..............	Ascending temperature	39.7	103	.78	1.85	49.93	—10	— 3	+44		
12	6.5 gm. N.........	Continued temperature	39.9	105	.81	1.93	51.15	— 2	+ 1	....	+ 8.9	Nov. 13.
13	Basal............	Continued temperature	39.8	107	.78	1.78	47.00	— 2	— 2	+35		
20	Basal............	Continued temperature	39.2	99	.76	1.76	45.52	— 2	— 0	+31		
Dec. 1	115 gm. glucose....	5th day, normal temp.	37.0	97	.97	1.54	40.10	— 8	......	....	+14.1	Dec. 2.
2	Basal............	6th day, normal temp.	36.9	76	.94	1.35	35.15	+ 6	......	+ 1		
5	10.2 gm. N........	9th day, normal temp.	37.1	91	.85	1.79	47.25	— 2	......	....	+24.3	Dec. 6.
6	Basal............	10th day, normal temp.	37.0	75	.96	1.45	38.03	+ 0	......	+10		
18	Basal............	22d day,* normal temp.	37.2	107	.84	1.60	48.28	+ 1	+ 1	+25		
30	Basal............	34th day,*normal temp.	37.2	108	.82	1.52	42.08	— 2	+ 3	+21		

Karl S. Jan. 6, 1914	Basal...............	Continued temperature	39.9	112	.76	1.74	54.01	— 3	— 6	+56		
6	10.5 gm. N.........	Continued temperature	39.9	108	.82	1.88	57.93	+ 3	+ 6	....	+ 7.3	Jan. 5.
16	Basal..............	Late steep curve......	38,2	95	.79	1.57	46.76	......	......	+35		
19	Basal..............	1st day, normal temp.	36.5	77	.88	1.19	35.83	......	......	+ 3		
21	10.0 gm. N.........	3d day, normal temp.	36.6	72	.90	1.33	40.06	......	......	....	+21.1	Jan. 22.
22	Basal..............	4th day, normal temp.	36.5	61	.89	1.10	33.08	......	......	— 5		
Feb. 6	Basal..............	18th day, normal temp.	36.9	81	.81	1.33	40.51	— 8	— 6	+17		
7	9.6 gm. N..........	19th day, normal temp.	37.0	90	.90	1.37	42.08	— 5	+ 2	....	+ 3.9	Feb. 6.
Thomas B. Oct. 15, 1913	* Basal..............	Late steep curve........	37.1	85	.82	1.07	36.54	— 6	......	+ 5		
21	Basal..............	1st day, normal temp.	36.9	78	.92	0.93	31.57	+ 2	......	— 9		
Richard T. Oct. 18, 1913	Basal..............	Early steep curve.......	39.0	90	.81	1.69	45.44	— 4	......	+31		
20	Basal..............	Early steep curve.......	38.3	93	.85	1.62	43.32	— 5	......	+25		
Anton K. Oct. 16, 1913	Basal..............	Late steep curve........	37.1	79	.86	1.27	38.26	+ 5	......	+10		
Rose G. Nov. 22, 1913	Basal..............	25th day, normal temp.	37.1	78	.87	1.71	43.13	+ 1	......	+24		
Edward B. Oct. 23, 1914	Basal..............	First relapse: early steep curve	38.5	116	.79	1.43	44.33	— 7	......	+28		
26	79 gm. olive oil...	First relapse: late steep curve	37.9	118	.81	1.33	41.50	— 2	......	....	+ 3.4	Oct. 27.
27	Basal..............	First relapse: late steep curve	37.6	107	.79	1.29	40.15	— 7	......	+16		
Nov. 4	Basal..............	4th day, normal temp.	37.2	104	.85	1.22	38.39	— 3	......	+12		
6	Basal..............	Second relapse: ascending temp.	39.3	124	.82	1.31	41.47	— 5	......	+20		
10	Basal (irrational)	Second relapse: continued temp.	40.3	141	.76	1.67	52.18	— 6	......	+50		
John K. Dec. 15, 1914	Basal..............	Continued temperature	39.2	63	.77	1.49	48.18	— 4	......	+39		

* Excluded from averages on account of rapid, irregular and weak heart action.

amounts of heat. Therefore the law of the conservation of energy applies to fever patients.

The rectal temperature does not always give an accurate indication of the average change in body temperature, and better results are often obtained by well covered surface thermometers.

The basal heat production rises and falls in a curve roughly parallel with the temperature. At the height of the fever it averages about 40 per cent. above the normal but in some cases rises to more than 50 per cent. above the normal.

The specific dynamic action of protein and carbohydrate is much smaller in the febrile period of typhoid than in health and in some cases seems to be absent. In convalescence it may be greater than normal.

In a majority of cases a rise in temperature is accompanied by an increasing heat production and an increasing heat elimination.

Typhoid patients can store body fat on an abundant diet while losing body weight and body protein. Loss in weight and loss of protein are usually though not necessarily parallel.

There is a toxic destruction of protein in typhoid fever. This is shown by the fact that patients have a distinctly negative nitrogen balance on a diet which contains more than enough calories to cover the heat production.

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CLINICAL CALORIMETRY

EIGHTH PAPER

ON THE DIABETIC RESPIRATORY QUOTIENT *

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The respiratory quotient, or the ratio of the volume of carbon dioxid expired to the volume of oxygen inspired, in the case of protein oxidation is stated by Loewy[1] to be 0.801. This relation depends on the net result of the oxidation of the many amino-acids of which protein is composed. It is apparent that when some of these amino-acids are converted into glucose which is eliminated in the urine, the respiratory quotient for protein will not hold true. It has been shown[2] that the carbon of glycocoll and alanin is completely converted into glucose in the diabetic organism, and that three of the carbon atoms which are contained in aspartic and glutamic acids are similarly convertible into glucose. Dakin[3] states that prolin and arginin yield glucose comparable in quantity to that yielded by glutamic acid. According to this author cystin and serin also yield glucose.

The reactions involving the conversion of amino-acids into sugar and urea may thus be written:[4]

Glycocoll .... $6CH_2NH_2.COOH + 3CO_2 + 3H_2O = 2C_6H_{12}O_6 + 3CH_4N_2O + 3O_2$

Alanin .... $2CH_3.CHNH_2.COOH + CO_2 + H_2O = C_6H_{12}O_6 + CH_4N_2O$

Aspartic Acid..... $2COOH.CH_2.CHNH_2.COOH + H_2O = C_6H_{12}O_6 + CH_4N_2O + CO_2$

Glutamic Acid..... $2COOH.CH_2.CH_2.CHNH_2COOH + 3O_2 = C_6H_{12}O_6 + CH_4N_2O + 3CO_2 + H_2O$

Prolin .... $2\underbrace{CH_2.CH_2.CH_2.CH}_{NH}.COOH + 5O_2 = C_6H_{12}O_6 + CH_4N_2O + 3CO_2 + H_2O$

Arginin .... $2NH_2.\underset{\underset{NH}{\|}}{C}.NH.CH_2.CH_2.CH_2.CHNH_2COOH + 5O_2 = C_6H_{12}O_6 + 4CH_4N_2O + 2CO_2$

Osborne and Jones[5] have reported an analysis of 100 grams of ox meat containing 16.18 per cent. of total nitrogen. This analysis will

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1. Loewy: Handb. d. Biochem., 1911, iv, No. 1, 279.
2. Ringer and Lusk: Ztschr. f. physiol. Chem., 1910, lxvi, 106.
3. Dakin: Jour. Biol. Chem., 1913, xiv, 321.
4. For more complete theoretical details consult: Lusk, Jour. Am. Chem. Soc., 1910, xxxii, 671; and Dakin and Dudley, Proc. Seventeenth Internat. Cong. Med., 1914, Sec. ii, Part II, 127.
5. Osborne and Jones: Am. Jour. Physiol., 1909, xxiv, 438.

be found below together with the respiratory quotients, both normal and diabetic, of the individual amino-acids.

TABLE 1.—ANALYSIS OF 100 GRAMS OX MEAT WITH RESPIRATORY QUOTIENTS

Substance	In 100 Gm. Meat gm.	Respiratory Quotient	
		Normal	Diabetic
Glycocoll	2.06	1.00	*
Alanin	3.72	0.83	*
Valin	0.81	0.75	
Leucin	11.65	0.73	
Prolin	5.82	0.82	0.60
Phenylalanin	3.15	0.87	
Aspartic acid	4.51	1.17	†
Glutamic acid	15.49	1.00	1.00
Serin	?	....	
Tyrosin	2.20	0.89	
Arginin	7.47	0.73	0.40
Histidin	1.76	0.90	
Lysin	7.59	0.71	
Ammonia	1.07		
Tryptophan	Present	0.87	
Total	67.30		

* R. Q. depressed below that of fat if glycocoll or alanin be ingested.
† R. Q. increased above that of fat if aspartic acid be given.

A glance at the above table shows how the respiratory quotient of 0.801 for protein is based on the sum of the results of the oxidation of many different substances, and also that the respiratory quotients usually tend to fall when certain of the amino-acids are converted into sugar.

A clear idea of this fall in the respiratory quotient can only be obtained if the respiratory metabolism of those amino-acids which are convertible into glucose is contrasted, the normal with the diabetic condition.

It will be noted in the foregoing table that only 67 per cent. of the ox protein was recovered as amino-acids. This is explained by the deficiency in the method; for Osborne and Jones[6] have analyzed a specially prepared mixture containing known quantities of a large number of amino-acids and have recovered only 66 per cent. of the substances present. As regards those amino-acids which are convertible into glucose, the following percentages were recovered from the mixture: Alanin, 46 per cent., prolin 73 per cent., aspartic acid, 42.5 per cent., glutamic acid 69 per cent., arginin 65 per cent. If one assumes that the quantity of glycocoll is at least double that found,

6. Osborne and Jones: Am. Jour. Physiol., 1910, xxvi, 325.

one arrives at values from which one may compute the quantity of sugar which should in theory arise from these acids. This appears in Table 2.

Since the 100 gm. of the ox muscle analyzed contained 16.18 gm. of nitrogen, the D:N equals 2.75:1.

TABLE 2.—CALCULATION SHOWING THE ORIGIN OF GLUCOSE FROM PROTEIN

Substance	Osborne	Recalculated	Glucose
Glycocoll	2.06	4.0	3.2
Alanin	3.72	8.1	8.2
Aspartic acid	4.51	10.6	7.2
Glutamic acid	15.49	22.3	13.6
Prolin	5.82	8.0	6.3
Arginin	7.47	11.5	5.9
		64.5	44.4

TABLE 3.—RESPIRATORY EXCHANGE IN THE NORMAL AND DIABETIC CONDITION OF SIX AMINO-ACIDS, AS THEY ARE CONTAINED IN 100 GM. OF OX MEAT, AND WHICH ARE CONVERTIBLE INTO 44.4 GM. OF GLUCOSE, D:N = 2.75

Substance	Grams	Normal		Diabetic			
				Oxygen		Carbon Dioxid	
		Oxygen gm.	Carbon Dioxid gm.	Absorbed gm.	Eliminated in Reaction gm.	Absorbed in Reaction gm.	Eliminated gm.
Glycocoll ...	4.0	2.56	3.52	.....	0.85	1.17	
Alanin	8.1	8.75	10.01	0.0	.....	2.00	
Aspartic acid	10.6	7.65	12.27	0.0	.....	....	1.75
Glutamic acid	22.3	21.85	30.04	7.30	.....	....	10.03
Prolin	8.0	12.25	13.77	5.57	.....	....	4.59
Arginin	11.5	11.63	11.63	5.32	.....	....	2.91
				18.19	0.85	3.17	19.28
				0.85	....	....	3.17
	64.5	64.69	81.24	17.34			16.11
R. Q.		0.915			0.675		

When the D:N ratio is 3.65, 59 gm. of glucose, or 14.6 gm. more than the quantity above estimated, are eliminated in the urine when 100 gm. of protein are destroyed. These 14.6 gm. represent an additional amount of glucose whose origin is unexplained and which is equal to 24 per cent. of the total maximal production. Such sources of sugar might be cystin, which if all the sulphur in protein were in that form

might at most yield 2 gm. of glucose and serin whose solubility has prevented any accuracy of determination.

Having determined the approximate quantities of the various sugar yielding amino-acids, one may now compute the difference between their oxidation normally and in the diabetic. This is shown in Table 3.

This table signifies that when glycocoll, alanin, aspartic acid, glutamic acid, prolin and arginin, together aggregating nearly two-thirds by weight of the protein complex, are oxidized in the normal organism in the proportion in which they may exist in meat, the respiratory quotient is 0.915, whereas if 44.4 gm. of glucose is formed from them the respiratory quotient sinks to only 0.675.

Of those amino-acids which do not yield glucose, three, valin, leucin and lysin, which together aggregate 20 gm. according to Osborne's (uncorrected) analysis of 100 gm. of meat, have respiratory quotients of 0.75, 0.73 and 0.71, respectively, whereas three others, phenylalanin, tyrosin and histidin, together amounting to only 7.1 gm., yield respiratory quotients of 0.87, 0.89 and 0.90. Furthermore, the 1.07 gm. of ammonia liberated would tend to reduce the quotient through urea formation. It is therefore obvious that the respiratory quotient for protein in diabetes is made up predominately of the oxidation of the remnants of the sugar forming amino-acids and from the oxidation of other amino-acids having in the main respiratory quotients of 0.75 to 0.71. As actually calculated, the above named mixture of non-sugar producing amino-acids would yield 48.25 gm. of CO_2 and require 45.86 gm. of oxygen for oxidation, showing a respiratory quotient of 0.76.

The aggregate quotient of the non-sugar forming amino-acids as set forth above may be indirectly obtained by deducting the estimated respiratory exchange of the sugar-forming amino-acids from that of the total involved in the normal oxidation of 100 gm. of ox protein, as shown in Table 4.

TABLE 4.—Aggregate Quotient of Non-Sugar Forming Amino-Acids

	Oxyen gm.	Carbon Dioxid gm.	Resp. Quot.
Normal oxidation of 100 grams of beef protein	138.18	152.17	0.801
Estimated oxidation of the sugar forming amino-acids	64.69	81.24	0.915
	73.49	70.93	
Add CO_2 for urea formation from 1.07 gm. NH_3	.....	1.39	
Estimated oxidation of non-sugar forming amino-acids	73.49	72.32	0.716

Although the last respiratory quotient 0.716 closely approximates that of leucin (0.73) and lysin (0.71), the dominant non-sugar forming amino-acids, it is evident that the influence of the other non-sugar

forming amino-acids would tend to raise the quotient to a higher level, to 0.76 in the before mentioned calculation. Therefore, the present figures can only be regarded as an attempted solution of the problem rather than as a precise analysis.

When the mixture of six sugar-forming amino-acids, aggregating 64.5 gm., is normally oxidized

$$O_2 = 64.69 \text{ gm. and } CO_2 = 81.24 \text{ gm.}$$

and when it is converted into 44.4 gm. of glucose

$$O_2 = 17.34 \text{ gm. and } CO_2 = 16.11 \text{ gm.}$$

the difference between these two sets of figures will represent the quantities of respiratory gases which would not be involved in the respiratory exchange in diabetes and would amount to

$$O_2 = 47.35 \text{ gm. and } CO_2 = 65.13 \text{ gm.}$$

If one takes the grams of respired gases in the normal combustion of 100 grams of protein as given by Loewy, and deducts from these the quantity not eliminated according to the above computation, one arrives at the following results for the diabetic respiratory quotient:

TABLE 5.—Protein Respiratory Quotient with D:N = 2.75

	Oxygen gm.	Carbon Dioxid gm.
Normal oxidation 100 grams beef protein................	138.18	152.17
Deduct for intermediary production of 44.4 grams of glucose	47.35	65.13
	90.83	87.04

R. Q. = 0.697.

Proceeding now to the consideration of the cases of diabetes in which the D:N is 3.65, calculations have been made the relations of which may be thus presented:

TABLE 6.—Protein Respiratory Quotient with D:N = 3.65

	Oxygen gm.	Carbon Dioxid gm.
(1). Normal oxidation of 100 grams of beef protein......	138.18	152.17
Deduction, if 16.28 grams N $\times$ 3.65 = 59.41 glucose.....	63.38	87.15
	74.80	65.02

R. Q. = 0.632.

The respiratory quotient for fat is 0.707, and since fat forms the main recourse of the diabetic, the respiratory quotient will be found nearer to that of fat than to 0.632 for protein. Thus, in a diabetic dog with a D:N ratio of 3.54 in which 23 per cent. of the total heat production was derived from protein and 77 per cent. from fat, the

respiratory quotient was 0.687, the non-protein respiratory quotient being 0.704, which closely approximates that of fat. In the case of a diabetic patient with a low protein metabolism whose urinary D:N was 3.6, Du Bois has found during a three hour period a respiratory quotient of 0.697. In another diabetic man with approximately the same D:N ratio but whose protein metabolism was higher (13 per cent. of the total energy) the R. Q. was 0.691.

Magnus-Levy[7] has called attention to a possible reduction in the respiratory quotient when beta-oxybutyric acid is formed from fat. He estimates that the maximal quantity of beta-oxybutyric acid derivable from 100 gm. of fat is 36 gm. Under these circumstances, the respiratory quotient for fat would be reduced from 0.707 to 0.669. The case is not so simple, however, for if the 36 gm. of acid formed neutralized sodium bicarbonate, 15.23 gm. of carbon dioxid would be eliminated.

These relations are shown in Table 7:

TABLE 7.—Theoretical Respiratory Quotient with Beta-Oxybutyric Acid Formed from Fat

	Oxygen Liters	Carbon Dioxid Liters	R. Q.
100 gm. fat	201.9	142.73	0.707
36 gm. beta-oxybutyric acid	34.85	30.96	0.889
	167.05	111.77	0.669
Add for 15.23 gm. CO_2 from $NaHCO_3$		7.74	
Possible end result	167.05	119.51	0.715

Since other bases than sodium bicarbonate may be used for the neutralization of beta-oxybutyric acid, it is apparent that the exact determination of the theoretical respiratory quotient when this acid is produced in large amounts in human diabetes is at present impossible.

This discussion has been prepared in order to further the understanding of a forthcoming description of metabolism in diabetes mellitus.

7. Magnus-Levy: Ztschr. f. klin. Med., 1905, lvi, 83.